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(54) Title: COMPOSITIONS AND METHODS FOR THERAPY AND DIAGNOSIS OF PROSTATE CANCER

#### (57) Abstract

Compositions and methods for the therapy and diagnosis of cancer, such as prostate cancer, are disclosed. Compositions may comprise one or more prostate tumor proteins, immunogenic portions thereof, or polynucleotides that encode such portions. Alternatively, a therapeutic composition may comprise an antigen presenting cell that expresses a prostate tumor protein, or a T cell that is specific for cells expressing such a protein. Such compositions may be used, for example, for the prevention and treatment of diseases such as prostate cancer. Diagnostic methods based on detecting a prostate tumor protein, or mRNA encoding such a protein, in a sample are also provided.

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# COMPOSITIONS AND METHODS FOR THERAPY AND DIAGNOSIS OF PROSTATE CANCER

#### **TECHNICAL FIELD**

The present invention relates generally to therapy and diagnosis of cancer, such as prostate cancer. The invention is more specifically related to polypeptides comprising at least a portion of a prostate tumor protein, and to polynucleotides encoding such polypeptides. Such polypeptides and polynucleotides may be used in vaccines and pharmaceutical compositions for prevention and treatment of prostate cancer, and for the diagnosis and monitoring of such cancers.

#### **BACKGROUND OF THE INVENTION**

Prostate cancer is the most common form of cancer among males, with an estimated incidence of 30% in men over the age of 50. Overwhelming clinical evidence shows that human prostate cancer has the propensity to metastasize to bone, and the disease appears to progress inevitably from androgen dependent to androgen refractory status, leading to increased patient mortality. This prevalent disease is currently the second leading cause of cancer death among men in the U.S.

In spite of considerable research into therapies for the disease, prostate cancer remains difficult to treat. Commonly, treatment is based on surgery and/or radiation therapy, but these methods are ineffective in a significant percentage of cases. Two previously identified prostate specific proteins - prostate specific antigen (PSA) and prostatic acid phosphatase (PAP) - have limited therapeutic and diagnostic potential. For example, PSA levels do not always correlate well with the presence of prostate cancer, being positive in a percentage of non-prostate cancer cases, including benign prostatic hyperplasia (BPH). Furthermore, PSA measurements correlate with prostate volume, and do not indicate the level of metastasis.

In spite of considerable research into therapies for these and other cancers, prostate cancer remains difficult to diagnose and treat effectively. Accordingly, there is a need in the art for improved methods for detecting and treating such cancers. The present invention fulfills these needs and further provides other related advantages.

#### SUMMARY OF THE INVENTION

Briefly stated, the present invention provides compositions and methods for the diagnosis and therapy of cancer, such as prostate cancer. In one aspect, the present invention provides polypeptides comprising at least a portion of a prostate tumor protein, or a variant thereof. Certain portions and other variants are immunogenic, such that the ability of the variant to react with antigen-specific antisera is not substantially diminished. Within certain embodiments, the polypeptide comprises at least an immunogenic portion of a prostate tumor protein, or a variant thereof, wherein the tumor protein comprises an amino acid sequence that is encoded by a polynucleotide sequence selected from the group consisting of: (a) sequences recited in any one of SEQ ID NOs:1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382 or 384-472; (b) sequences that hybridize to any of the foregoing sequences under moderately stringent conditions; and (c) complements of any of the sequence of (a) or (b). In certain specific embodiments, such a polypeptide comprises at least a portion, or variant thereof, of a tumor protein that includes an amino acid sequence selected from the group consisting of sequences recited in any one of SEQ ID NO: 112-114, 172, 176, 178, 327, 329, 331, 336, 339, 376-380 and 383.

The present invention further provides polynucleotides that encode a polypeptide as described above, or a portion thereof (such as a portion encoding at least 15 amino acid residues of a prostate tumor protein), expression vectors comprising such polynucleotides and host cells transformed or transfected with such expression vectors.

Within other aspects, the present invention provides pharmaceutical compositions comprising a polypeptide or polynucleotide as described above and a physiologically acceptable carrier.

Within a related aspect of the present invention, vaccines are provided. Such vaccines comprise a polypeptide or polynucleotide as described above and a non-specific immune response enhancer.

The present invention further provides pharmaceutical compositions that comprise: (a) an antibody or antigen-binding fragment thereof that specifically binds to a prostate tumor protein; and (b) a physiologically acceptable carrier.

Within further aspects, the present invention provides pharmaceutical compositions comprising: (a) an antigen presenting cell that expresses a polypeptide as described above and (b) a pharmaceutically acceptable carrier or excipient. Antigen presenting cells include dendritic cells, macrophages, monocytes, fibroblasts and B cells.

Within related aspects, vaccines are provided that comprise: (a) an antigen presenting cell that expresses a polypeptide as described above and (b) a non-specific immune response enhancer.

The present invention further provides, in other aspects, fusion proteins that comprise at least one polypeptide as described above, as well as polynucleotides encoding such fusion proteins.

Within related aspects, pharmaceutical compositions comprising a fusion protein, or a polynucleotide encoding a fusion protein, in combination with a physiologically acceptable carrier are provided.

Vaccines are further provided, within other aspects, that comprise a fusion protein, or a polynucleotide encoding a fusion protein, in combination with a non-specific immune response enhancer.

Within further aspects, the present invention provides methods for inhibiting the development of a cancer in a patient, comprising administering to a patient a pharmaceutical composition or vaccine as recited above.

The present invention further provides, within other aspects, methods for removing tumor cells from a biological sample, comprising contacting a biological sample with T cells that specifically react with a prostate tumor protein, wherein the step of contacting is performed under conditions and for a time sufficient to permit the removal of cells expressing the protein from the sample.

Within related aspects, methods are provided for inhibiting the development of a cancer in a patient, comprising administering to a patient a biological sample treated as described above.

Methods are further provided, within other aspects, for stimulating and/or expanding T cells specific for a prostate tumor protein, comprising contacting T cells with one or more of: (i) a polypeptide as described above; (ii) a polypucleotide encoding such a polypeptide; and/or (iii) an antigen presenting cell that expresses such a polypeptide; under conditions and for a time sufficient to permit the stimulation and/or expansion of T cells. Isolated T cell populations comprising T cells prepared as described above are also provided.

Within further aspects, the present invention provides methods for inhibiting the development of a cancer in a patient, comprising administering to a patient an effective amount of a T cell population as described above.

The present invention further provides methods for inhibiting the development of a cancer in a patient, comprising the steps of: (a) incubating CD4+ and/or CD8+ T cells isolated from a patient with one or more of: (i) a polypeptide comprising at least an immunogenic portion of a prostate tumor protein; (ii) a polypucleotide encoding such a polypeptide; and (iii) an antigen-presenting cell that expressed such a polypeptide; and (b) administering to the patient an effective amount of the proliferated T cells, and thereby inhibiting the development of a cancer in the patient. Proliferated cells may, but need not, be cloned prior to administration to the patient.

Within further aspects, the present invention provides methods for determining the presence or absence of a cancer in a patient, comprising: (a) contacting a biological sample obtained from a patient with a binding agent that binds to a polypeptide as recited above; (b) detecting in the sample an amount of polypeptide that binds to the binding agent; and (c) comparing the amount of polypeptide with a predetermined cut-off value, and therefrom determining the presence or absence of a cancer in the patient. Within preferred embodiments, the binding agent is an antibody, more preferably a monoclonal antibody. The cancer may be prostate cancer.

The present invention also provides, within other aspects, methods for monitoring the progression of a cancer in a patient. Such methods comprise the steps of: (a) contacting a biological sample obtained from a patient at a first point in time with a binding agent that binds to a polypeptide as recited above; (b) detecting in the sample an amount of polypeptide that binds to the binding agent; (c) repeating steps (a) and (b) using a biological sample obtained from the patient at a subsequent point in time; and (d) comparing the amount of polypeptide detected in step (c) with the amount detected in step (b) and therefrom monitoring the progression of the cancer in the patient.

The present invention further provides, within other aspects, methods for determining the presence or absence of a cancer in a patient, comprising the steps of: (a) contacting a biological sample obtained from a patient with an oligonucleotide that hybridizes to a polynucleotide that encodes a prostate tumor protein; (b) detecting in the sample a level of a polynucleotide, preferably mRNA, that hybridizes to the oligonucleotide; and (c) comparing the level of polynucleotide that hybridizes to the oligonucleotide with a predetermined cut-off value, and therefrom determining the presence or absence of a cancer in the patient. Within certain embodiments, the amount of mRNA is detected via polymerase chain reaction using, for example, at least one oligonucleotide primer that hybridizes to a polynucleotide encoding a polypeptide as recited above, or a complement of such a polynucleotide. Within other embodiments, the amount of mRNA is detected using a hybridization technique, employing an oligonucleotide probe that hybridizes to a polynucleotide that encodes a polypeptide as recited above, or a complement of such a polynucleotide that encodes a polypeptide as recited above, or a complement of such a polynucleotide.

In related aspects, methods are provided for monitoring the progression of a cancer in a patient, comprising the steps of: (a) contacting a biological sample obtained from a patient with an oligonucleotide that hybridizes to a polynucleotide that encodes a prostate tumor protein; (b) detecting in the sample an amount of a polynucleotide that hybridizes to the oligonucleotide; (c) repeating steps (a) and (b) using a biological sample obtained from the patient at a subsequent point in time; and (d) comparing the amount of polynucleotide detected in step (c) with the amount detected in step (b) and therefrom monitoring the progression of the cancer in the patient.

Within further aspects, the present invention provides antibodies, such as monoclonal antibodies, that bind to a polypeptide as described above, as well as diagnostic

kits comprising such antibodies. Diagnostic kits comprising one or more oligonucleotide probes or primers as described above are also provided.

These and other aspects of the present invention will become apparent upon - reference to the following detailed description and attached drawings. All references disclosed herein are hereby incorporated by reference in their entirety as if each was incorporated individually.

# BRIEF DESCRIPTION OF THE DRAWINGS AND SEQUENCE IDENTIFIERS

Figure 1 illustrates the ability of T cells to kill fibroblasts expressing the representative prostate tumor polypeptide P502S, as compared to control fibroblasts. The percentage lysis is shown as a series of effector:target ratios, as indicated.

Figures 2A and 2B illustrate the ability of T cells to recognize cells expressing the representative prostate tumor polypeptide P502S. In each case, the number of  $\gamma$ -interferon spots is shown for different numbers of responders. In Figure 2A, data is presented for fibroblasts pulsed with the P2S-12 peptide, as compared to fibroblasts pulsed with a control E75 peptide. In Figure 2B, data is presented for fibroblasts expressing P502S, as compared to fibroblasts expressing HER-2/neu.

Figure 3 represents a peptide competition binding assay showing that the P1S#10 peptide, derived from P501S, binds HLA-A2. Peptide P1S#10 inhibits HLA-A2 restricted presentation of fluM58 peptide to CTL clone D150M58 in TNF release bioassay. D150M58 CTL is specific for the HLA-A2 binding influenza matrix peptide fluM58.

Figure 4 illustrates the ability of T cell lines generated from P1S#10 immunized mice to specifically lyse P1S#10-pulsed Jurkat A2Kb targets and P501S-transduced Jurkat A2Kb targets, as compared to EGFP-transduced Jurkat A2Kb. The percent lysis is shown as a series of effector to target ratios, as indicated.

Figure 5 illustrates the ability of a T cell clone to recognize and specifically lyse Jurkat A2Kb cells expressing the representative prostate tumor polypeptide P501S, thereby demonstrating that the P1S#10 peptide may be a naturally processed epitope of the P501S polypeptide.

Figures 6A and 6B are graphs illustrating the specificity of a CD8<sup>+</sup> cell line (3A-1) for a representative prostate tumor antigen (P501S). Figure 6A shows the results of a <sup>51</sup>Cr release assay. The percent specific lysis is shown as a series of effector:target ratios, as indicated. Figure 6B shows the production of interferon-gamma by 3A-1 cells stimulated with autologous B-LCL transduced with P501S, at varying effector:target rations as indicated.

SEQ ID NO: 1 is the determined cDNA sequence for F1-13

SEQ ID NO: 2 is the determined 3' cDNA sequence for F1-12

SEQ ID NO: 3 is the determined 5' cDNA sequence for F1-12 SEQ ID NO: 4 is the determined 3' cDNA sequence for F1-16 SEQ ID NO: 5 is the determined 3' cDNA sequence for H1-1 SEQ ID NO: 6 is the determined 3' cDNA sequence for H1-9 SEQ ID NO: 7 is the determined 3' cDNA sequence for H1-4 SEQ ID NO: 8 is the determined 3' cDNA sequence for J1-17 SEQ ID NO: 9 is the determined 5' cDNA sequence for J1-17 SEQ ID NO: 10 is the determined 3' cDNA sequence for L1-12 SEO ID NO: 11 is the determined 5' cDNA sequence for L1-12 SEQ ID NO: 12 is the determined 3' cDNA sequence for N1-1862 SEQ ID NO: 13 is the determined 5' cDNA sequence for N1-1862 SEQ ID NO: 14 is the determined 3' cDNA sequence for J1-13 SEQ ID NO: 15 is the determined 5' cDNA sequence for J1-13 SEQ ID NO: 16 is the determined 3' cDNA sequence for J1-19 SEQ ID NO: 17 is the determined 5' cDNA sequence for J1-19 SEQ ID NO: 18 is the determined 3' cDNA sequence for J1-25 SEQ ID NO: 19 is the determined 5' cDNA sequence for J1-25 SEQ ID NO: 20 is the determined 5' cDNA sequence for J1-24 SEQ ID NO: 21 is the determined 3' cDNA sequence for J1-24 SEQ ID NO: 22 is the determined 5' cDNA sequence for K1-58 SEQ ID NO: 23 is the determined 3' cDNA sequence for K1-58 SEQ ID NO: 24 is the determined 5' cDNA sequence for K1-63 SEQ ID NO: 25 is the determined 3' cDNA sequence for K1-63 SEQ ID NO: 26 is the determined 5' cDNA sequence for L1-4. SEQ ID NO: 27 is the determined 3' cDNA sequence for L1-4 SEQ ID NO: 28 is the determined 5' cDNA sequence for L1-14 SEQ ID NO: 29 is the determined 3' cDNA sequence for L1-14 SEQ ID NO: 30 is the determined 3' cDNA sequence for J1-12 SEQ ID NO: 31 is the determined 3' cDNA sequence for J1-16 SEQ ID NO: 32 is the determined 3' cDNA sequence for J1-21 SEQ ID NO: 33 is the determined 3' cDNA sequence for K1-48 SEQ ID NO: 34 is the determined 3' cDNA sequence for K1-55 SEQ ID NO: 35 is the determined 3' cDNA sequence for L1-2 SEQ ID NO: 36 is the determined 3' cDNA sequence for L1-6 SEQ ID NO: 37 is the determined 3' cDNA sequence for N1-1858 SEQ ID NO: 38 is the determined 3' cDNA sequence for N1-1860 SEQ ID NO: 39 is the determined 3' cDNA sequence for N1-1861

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SEQ ID NO: 112 is the predicted amino acid sequence for J1-17.

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SEQ ID NO: 222 is the determined cDNA sequence for g-f3rev
SEQ ID NO: 223 is the determined cDNA sequence for P509S

SEQ ID NO: 224 is the determined cDNA sequence for P510S SEO ID NO: 225 is the determined cDNA sequence for P703DE5 SEO ID NO: 226 is the determined cDNA sequence for 9-A11 SEO ID NO: 227 is the determined cDNA sequence for 8-C6 SEQ ID NO: 228 is the determined cDNA sequence for 8-H7 SEQ ID NO: 229 is the determined cDNA sequence for JPTPN13 SEQ ID NO: 230 is the determined cDNA sequence for JPTPN14 SEQ ID NO: 231 is the determined cDNA sequence for JPTPN23 SEQ ID NO: 232 is the determined cDNA sequence for JPTPN24 SEQ ID NO: 233 is the determined cDNA sequence for JPTPN25 SEQ ID NO: 234 is the determined cDNA sequence for JPTPN30 SEQ ID NO: 235 is the determined cDNA sequence for JPTPN34 SEQ ID NO: 236 is the determined cDNA sequence for PTPN35 SEQ ID NO: 237 is the determined cDNA sequence for JPTPN36 SEQ ID NO: 238 is the determined cDNA sequence for JPTPN38 SEQ ID NO: 239 is the determined cDNA sequence for JPTPN39 SEQ ID NO: 240 is the determined cDNA sequence for JPTPN40 SEQ ID NO: 241 is the determined cDNA sequence for JPTPN41 SEO ID NO: 242 is the determined cDNA sequence for JPTPN42 SEQ ID NO: 243 is the determined cDNA sequence for JPTPN45 SEQ ID NO: 244 is the determined cDNA sequence for JPTPN46 SEQ ID NO: 245 is the determined cDNA sequence for JPTPN51 SEQ ID NO: 246 is the determined cDNA sequence for JPTPN56 SEQ ID NO: 247 is the determined cDNA sequence for PTPN64 SEQ ID NO: 248 is the determined cDNA sequence for JPTPN65 SEQ ID NO: 249 is the determined cDNA sequence for JPTPN67 SEQ ID NO: 250 is the determined cDNA sequence for JPTPN76 SEQ ID NO: 251 is the determined cDNA sequence for JPTPN84 SEQ ID NO: 252 is the determined cDNA sequence for JPTPN85 SEQ ID NO: 253 is the determined cDNA sequence for JPTPN86 SEQ ID NO: 254 is the determined cDNA sequence for JPTPN87 SEQ ID NO: 255 is the determined cDNA sequence for JPTPN88 SEQ ID NO: 256 is the determined cDNA sequence for JP1F1 SEQ ID NO: 257 is the determined cDNA sequence for JP1F2 SEQ ID NO: 258 is the determined cDNA sequence for JP1C2 SEQ ID NO: 259 is the determined cDNA sequence for JP1B1 SEQ ID NO: 260 is the determined cDNA sequence for JP1B2

SEQ ID NO: 261 is the determined cDNA sequence for JP1D3 SEQ ID NO: 262 is the determined cDNA sequence for JP1A4 SEQ ID NO: 263 is the determined cDNA sequence for JP1F5 SEQ ID NO: 264 is the determined cDNA sequence for JP1E6 SEQ ID NO: 265 is the determined cDNA sequence for JP1D6 SEQ ID NO: 266 is the determined cDNA sequence for JP1B5 SEQ ID NO: 267 is the determined cDNA sequence for JP1A6 SEQ ID NO: 268 is the determined cDNA sequence for JP1E8 SEQ ID NO: 269 is the determined cDNA sequence for JP1D7 SEQ ID NO: 270 is the determined cDNA sequence for JP1D9 SEQ ID NO: 271 is the determined cDNA sequence for JP1C10 SEQ ID NO: 272 is the determined cDNA sequence for JP1A9 SEQ ID NO: 273 is the determined cDNA sequence for JP1F12 SEQ ID NO: 274 is the determined cDNA sequence for JP1E12 SEQ ID NO: 275 is the determined cDNA sequence for JP1D11 SEQ ID NO: 276 is the determined cDNA sequence for JP1C11 SEQ ID NO: 277 is the determined cDNA sequence for JP1C12 SEQ ID NO: 278 is the determined cDNA sequence for JP1B12 SEQ ID NO: 279 is the determined cDNA sequence for JP1A12 SEQ ID NO: 280 is the determined cDNA sequence for JP8G2 SEQ ID NO: 281 is the determined cDNA sequence for JP8H1 SEQ ID NO: 282 is the determined cDNA sequence for JP8H2 SEQ ID NO: 283 is the determined cDNA sequence for JP8A3. SEQ ID NO: 284 is the determined cDNA sequence for JP8A4 SEQ ID NO: 285 is the determined cDNA sequence for JP8C3 SEQ ID NO: 286 is the determined cDNA sequence for JP8G4 SEQ ID NO: 287 is the determined cDNA sequence for JP8B6 SEQ ID NO: 288 is the determined cDNA sequence for JP8D6 SEQ ID NO: 289 is the determined cDNA sequence for JP8F5 SEQ ID NO: 290 is the determined cDNA sequence for JP8A8 SEQ ID NO: 291 is the determined cDNA sequence for JP8C7 SEQ ID NO: 292 is the determined cDNA sequence for JP8D7 SEQ ID NO: 293 is the determined cDNA sequence for P8D8 SEQ ID NO: 294 is the determined cDNA sequence for JP8E7 SEQ ID NO: 295 is the determined cDNA sequence for JP8F8 SEQ ID NO: 296 is the determined cDNA sequence for JP8G8 SEQ ID NO: 297 is the determined cDNA sequence for JP8B10

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SEO ID NO: 298 is the determined cDNA sequence for JP8C10
SEQ ID NO: 299 is the determined cDNA sequence for JP8E9
SEO ID NO: 300 is the determined cDNA sequence for JP8E10
SEQ ID NO: 301 is the determined cDNA sequence for JP8F9
SEQ ID NO: 302 is the determined cDNA sequence for JP8H9
SEQ ID NO: 303 is the determined cDNA sequence for JP8C12
SEQ ID NO: 304 is the determined cDNA sequence for JP8E11
SEO ID NO: 305 is the determined cDNA sequence for JP8E12
SEQ ID NO: 306 is the amino acid sequence for the peptide PS2#12
SEO ID NO: 307 is the determined cDNA sequence for P711P
SEQ ID NO: 308 is the determined cDNA sequence for P712P
SEQ ID NO: 309 is the determined cDNA sequence for CLONE23
SEQ ID NO: 310 is the determined cDNA sequence for P774P
SEQ ID NO: 311 is the determined cDNA sequence for P775P
SEQ ID NO: 312 is the determined cDNA sequence for P715P
SEQ ID NO: 313 is the determined cDNA sequence for P710P
SEQ ID NO: 314 is the determined cDNA sequence for P767P
SEQ ID NO: 315 is the determined cDNA sequence for P768P
SEO ID NO: 316-325 are the determined cDNA sequences of previously isolated genes
SEQ ID NO: 326 is the determined cDNA sequence for P703PDE5
SEQ ID NO: 327 is the predicted amino acid sequence for P703PDE5
SEQ ID NO: 328 is the determined cDNA sequence for P703P6.26
SEQ ID NO: 329 is the predicted amino acid sequence for P703P6.26
SEQ ID NO: 330 is the determined cDNA sequence for P703PX-23
SEQ ID NO: 331 is the predicted amino acid sequence for P703PX-23
SEQ ID NO: 332 is the determined full length cDNA sequence for P509S
SEQ ID NO: 333 is the determined extended cDNA sequence for P707P (also referred to as
11-C9)
SEQ ID NO: 334 is the determined cDNA sequence for P714P
SEQ ID NO: 335 is the determined cDNA sequence for P705P (also referred to as 9-F3)
SEQ ID NO: 336 is the predicted amino acid sequence for P705P
SEQ ID NO: 337 is the amino acid sequence of the peptide P1S#10
SEQ ID NO: 338 is the amino acid sequence of the peptide p5
SEQ ID NO: 339 is the predicted amino acid sequence of P509S
SEQ ID NO: 340 is the determined cDNA sequence for P778P
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SEQ ID NO: 341 is the determined cDNA sequence for P786P SEQ ID NO: 342 is the determined cDNA sequence for P789P

SEQ ID NO: 343 is the determined cDNA sequence for a clone showing homology to Homo sapiens MM46 mRNA

SEQ ID NO: 344 is the determined cDNA sequence for a clone showing homology to Homo sapiens TNF-alpha stimulated ABC protein (ABC50) mRNA

SEQ ID NO: 345 is the determined cDNA sequence for a clone showing homology to Homo sapiens mRNA for E-cadherin

SEQ ID NO: 346 is the determined cDNA sequence for a clone showing homology to Human nuclear-encoded mitochondrial serine hydroxymethyltransferase (SHMT)

SEQ ID NO: 347 is the determined cDNA sequence for a clone showing homology to Homo sapiens natural resistance-associated macrophage protein2 (NRAMP2)

SEQ ID NO: 348 is the determined cDNA sequence for a clone showing homology to Homo sapiens phosphoglucomutase-related protein (PGMRP)

SEQ ID NO: 349 is the determined cDNA sequence for a clone showing homology to Human mRNA for proteosome subunit p40

SEQ ID NO: 350 is the determined cDNA sequence for P777P

SEQ ID NO: 351 is the determined cDNA sequence for P779P

SEQ ID NO: 352 is the determined cDNA sequence for P790P

SEQ ID NO: 353 is the determined cDNA sequence for P784P SEQ ID NO: 354 is the determined cDNA sequence for P776P

SEQ ID NO: 355 is the determined cDNA sequence for P780P

SEQ ID NO: 356 is the determined cDNA sequence for P544S

SEQ ID NO: 357 is the determined cDNA sequence for P745S

SEQ ID NO: 358 is the determined cDNA sequence for P782P

SEQ ID NO: 359 is the determined cDNA sequence for P783P

SEQ ID NO: 360 is the determined cDNA sequence for unknown 17984

SEQ ID NO: 361 is the determined cDNA sequence for P787P

SEQ ID NO: 362 is the determined cDNA sequence for P788P

SEQ ID NO: 363 is the determined cDNA sequence for unknown 17994

SEQ ID NO: 364 is the determined cDNA sequence for P781P

SEQ ID NO: 365 is the determined cDNA sequence for P785P

SEQ ID NO: 366-375 are the determined cDNA sequences for splice variants of B305D.

SEQ ID NO: 376 is the predicted amino acid sequence encoded by the sequence of SEQ ID NO: 366.

SEQ ID NO: 377 is the predicted amino acid sequence encoded by the sequence of SEQ ID NO: 372.

SEQ ID NO: 378 is the predicted amino acid sequence encoded by the sequence of SEQ ID NO: 373.

SEQ ID NO: 379 is the predicted amino acid sequence encoded by the sequence of SEQ ID

NO: 374.

SEQ ID NO: 380 is the predicted amino acid sequence encoded by the sequence of SEQ ID

NO: 375.

SEQ ID NO: 381 is the determined cDNA sequence for B716P.

SEQ ID NO: 382 is the determined full-length cDNA sequence for P711P.

SEQ ID NO: 383 is the predicted amino acid sequence for P711P.

SEQ ID NO: 384 is the cDNA sequence for P1000C.

SEQ ID NO: 385 is the cDNA sequence for CGI-82.

SEQ ID NO:386 is the cDNA sequence for 23320.

SEQ ID NO:387 is the cDNA sequence for CGI-69.

SEQ ID NO:388 is the cDNA sequence for L-iditol-2-dehydrogenase.

SEQ ID NO:389 is the cDNA sequence for 23379.

SEQ ID NO:390 is the cDNA sequence for 23381.

SEQ ID NO:391 is the cDNA sequence for KIAA0122.

SEQ ID NO:392 is the cDNA sequence for 23399.

SEQ ID NO:393 is the cDNA sequence for a previously identified gene.

SEQ ID NO:394 is the cDNA sequence for HCLBP.

SEQ ID NO:395 is the cDNA sequence for transglutaminase.

SEQ ID NO:396 is the cDNA sequence for a previously identified gene.

SEQ ID NO:397 is the cDNA sequence for PAP.

SEQ ID NO:398 is the cDNA sequence for Ets transcription factor PDEF.

SEQ ID NO:399 is the cDNA sequence for hTGR.

SEQ ID NO:400 is the cDNA sequence for KIAA0295.

SEQ ID NO:401 is the cDNA sequence for 22545.

SEQ ID NO:402 is the cDNA sequence for 22547.

SEQ ID NO:403 is the cDNA sequence for 22548.

SEQ ID NO:404 is the cDNA sequence for 22550.

SEQ ID NO:405 is the cDNA sequence for 22551.

SEQ ID NO:406 is the cDNA sequence for 22552.

SEQ ID NO:407 is the cDNA sequence for 22553.

SEQ ID NO:408 is the cDNA sequence for 22558.

SEQ ID NO:409 is the cDNA sequence for 22562.

SEQ ID NO:410 is the cDNA sequence for 22565.

SEQ ID NO:411 is the cDNA sequence for 22567.

SEQ ID NO:412 is the cDNA sequence for 22568.

SEQ ID NO:413 is the cDNA sequence for 22570.

SEQ ID NO:414 is the cDNA sequence for 22571. SEQ ID NO:415 is the cDNA sequence for 22572. SEQ ID NO:416 is the cDNA sequence for 22573. SEQ ID NO:417 is the cDNA sequence for 22573. SEQ ID NO:418 is the cDNA sequence for 22575. SEQ ID NO:419 is the cDNA sequence for 22580. SEQ ID NO:420 is the cDNA sequence for 22581. SEQ ID NO:421 is the cDNA sequence for 22582. SEQ ID NO:422 is the cDNA sequence for 22583. SEQ ID NO:423 is the cDNA sequence for 22584. SEQ ID NO:424 is the cDNA sequence for 22585. SEQ ID NO:425 is the cDNA sequence for 22586. SEQ ID NO:426 is the cDNA sequence for 22587. SEQ ID NO:427 is the cDNA sequence for 22588. SEQ ID NO:428 is the cDNA sequence for 22589. SEQ ID NO:429 is the cDNA sequence for 22590. SEQ ID NO:430 is the cDNA sequence for 22591. SEQ ID NO:431 is the cDNA sequence for 22592. SEQ ID NO:432 is the cDNA sequence for 22593. SEQ ID NO:433 is the cDNA sequence for 22594. SEQ ID NO:434 is the cDNA sequence for 22595. SEQ ID NO:435 is the cDNA sequence for 22596. SEQ ID NO:436 is the cDNA sequence for 22847. SEQ ID NO:437 is the cDNA sequence for 22848. SEQ ID NO:438 is the cDNA sequence for 22849. SEQ ID NO:439 is the cDNA sequence for 22851. SEQ ID NO:440 is the cDNA sequence for 22852. SEQ ID NO:441 is the cDNA sequence for 22853. SEQ ID NO:442 is the cDNA sequence for 22854. SEQ ID NO:443 is the cDNA sequence for 22855. SEQ ID NO:444 is the cDNA sequence for 22856. SEQ ID NO:445 is the cDNA sequence for 22857. SEQ ID NO:446 is the cDNA sequence for 23601. SEQ ID NO:447 is the cDNA sequence for 23602. SEQ ID NO:448 is the cDNA sequence for 23605. SEQ ID NO:449 is the cDNA sequence for 23606. SEQ ID NO:450 is the cDNA sequence for 23612.

SEQ ID NO:451 is the cDNA sequence for 23614.

SEQ ID NO:452 is the cDNA sequence for 23618.

SEQ ID NO:453 is the cDNA sequence for 23622.

SEQ ID NO:454 is the cDNA sequence for folate hydrolase.

SEQ ID NO:455 is the cDNA sequence for LIM protein.

SEQ ID NO:456 is the cDNA sequence for a known gene.

SEQ ID NO:457 is the cDNA sequence for a known gene.

SEQ ID NO:458 is the cDNA sequence for a previously identified gene.

SEQ ID NO:459 is the cDNA sequence for 23045.

SEQ ID NO:460 is the cDNA sequence for 23032.

SEQ ID NO:461 is the cDNA sequence for 23054.

SEQ ID NOs:462-467 are cDNA sequences for known genes.

SEQ ID NOs:468-471 are cDNA sequences for P710P.

SEQ ID NO:472 is a cDNA sequence for P1001C.

# DETAILED DESCRIPTION OF THE INVENTION

As noted above, the present invention is generally directed to compositions and methods for the therapy and diagnosis of cancer, such as prostate cancer. The compositions described herein may include prostate tumor polypeptides, polynucleotides encoding such polypeptides, binding agents such as antibodies, antigen presenting cells (APCs) and/or immune system cells (e.g., T cells). Polypeptides of the present invention generally comprise at least a portion (such as an immunogenic portion) of a prostate tumor protein or a variant thereof. A "prostate tumor protein" is a protein that is expressed in prostate tumor cells at a level that is at least two fold, and preferably at least five fold, greater than the level of expression in a normal tissue, as determined using a representative assay provided herein. Certain prostate tumor proteins are tumor proteins that react detectably (within an immunoassay, such as an ELISA or Western blot) with antisera of a patient afflicted with prostate cancer. Polynucleotides of the subject invention generally comprise a DNA or RNA sequence that encodes all or a portion of such a polypeptide, or that is complementary to such a sequence. Antibodies are generally immune system proteins, or antigen-binding fragments thereof, that are capable of binding to a polypeptide as described above. Antigen presenting cells include dendritic cells, macrophages, monocytes, fibroblasts and B-cells that express a polypeptide as described above. T cells that may be employed within such compositions are generally T cells that are specific for a polypeptide as described above.

The present invention is based on the discovery of human prostate tumor proteins. Sequences of polynucleotides encoding certain tumor proteins, or portions thereof, are provided in SEQ ID NOs:1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382 or 384-472. Sequences of polypeptides comprising at least a portion of a tumor protein are provided in SEQ ID NOs:112-114, 172, 176, 178, 327, 329, 331, 336, 339, 376-380 and 383.

#### PROSTATE TUMOR PROTEIN POLYNUCLEOTIDES

Any polynucleotide that encodes a prostate tumor protein or a portion or other variant thereof as described herein is encompassed by the present invention. Preferred polynucleotides comprise at least 15 consecutive nucleotides, preferably at least 30 consecutive nucleotides and more preferably at least 45 consecutive nucleotides, that encode a portion of a prostate tumor protein. More preferably, a polynucleotide encodes an immunogenic portion of a prostate tumor protein. Polynucleotides complementary to any such sequences are also encompassed by the present invention. Polynucleotides may be single-stranded (coding or antisense) or double-stranded, and may be DNA (genomic, cDNA or synthetic) or RNA molecules. RNA molecules include HnRNA molecules, which contain introns and correspond to a DNA molecule in a one-to-one manner, and mRNA molecules, which do not contain introns. Additional coding or non-coding sequences may, but need not, be present within a polynucleotide of the present invention, and a polynucleotide may, but need not, be linked to other molecules and/or support materials.

Polynucleotides may comprise a native sequence (i.e., an endogenous sequence that encodes a prostate tumor protein or a portion thereof) or may comprise a variant of such a sequence. Polynucleotide variants may contain one or more substitutions, additions, deletions and/or insertions such that the immunogenicity of the encoded polypeptide is not diminished, relative to a native tumor protein. The effect on the immunogenicity of the encoded polypeptide may generally be assessed as described herein. Variants preferably exhibit at least about 70% identity, more preferably at least about 80% identity and most preferably at least about 90% identity to a polynucleotide sequence that encodes a native prostate tumor protein or a portion thereof.

Two polynucleotide or polypeptide sequences are said to be "identical" if the sequence of nucleotides or amino acids in the two sequences is the same when aligned for maximum correspondence as described below. Comparisons between two sequences are typically performed by comparing the sequences over a comparison window to identify and compare local regions of sequence similarity. A "comparison window" as used herein, refers to a segment of at least about 20 contiguous positions, usually 30 to about 75, 40 to about 50,

in which a sequence may be compared to a reference sequence of the same number of contiguous positions after the two sequences are optimally aligned.

Optimal alignment of sequences for comparison may be conducted using the Megalign program in the Lasergene suite of bioinformatics software (DNASTAR, Inc., Madison, WI), using default parameters. This program embodies several alignment schemes described in the following references: Dayhoff, M.O. (1978) A model of evolutionary change in proteins – Matrices for detecting distant relationships. In Dayhoff, M.O. (ed.) Atlas of Protein Sequence and Structure, National Biomedical Research Foundation, Washington DC Vol. 5, Suppl. 3, pp. 345-358; Hein J. (1990) Unified Approach to Alignment and Phylogenes pp. 626-645 Methods in Enzymology vol. 183, Academic Press, Inc., San Diego, CA; Higgins, D.G. and Sharp, P.M. (1989) CABIOS 5:151-153; Myers, E.W. and Muller W. (1988) CABIOS 4:11-17; Robinson, E.D. (1971) Comb. Theor 11:105; Santou, N. Nes, M. (1987) Mol. Biol. Evol. 4:406-425; Sneath, P.H.A. and Sokal, R.R. (1973) Numerical Taxonomy – the Principles and Practice of Numerical Taxonomy, Freeman Press, San Francisco, CA; Wilbur, W.J. and Lipman, D.J. (1983) Proc. Natl. Acad., Sci. USA 80:726-730.

Preferably, the "percentage of sequence identity" is determined by comparing two optimally aligned sequences over a window of comparison of at least 20 positions, wherein the portion of the polynucleotide or polypeptide sequence in the comparison window may comprise additions or deletions (i.e., gaps) of 20 percent or less, usually 5 to 15 percent, or 10 to 12 percent, as compared to the reference sequences (which does not comprise additions or deletions) for optimal alignment of the two sequences. The percentage is calculated by determining the number of positions at which the identical nucleic acid bases or amino acid residue occurs in both sequences to yield the number of matched positions, dividing the number of matched positions by the total number of positions in the reference sequence (i.e., the window size) and multiplying the results by 100 to yield the percentage of sequence identity.

Variants may also, or alternatively, be substantially homologous to a native gene, or a portion or complement thereof. Such polynucleotide variants are capable of hybridizing under moderately stringent conditions to a naturally occurring DNA sequence encoding a native prostate tumor protein (or a complementary sequence). Suitable moderately stringent conditions include prewashing in a solution of 5 X SSC, 0.5% SDS, 1.0 mM EDTA (pH 8.0); hybridizing at 50°C-65°C, 5 X SSC, overnight; followed by washing twice at 65°C for 20 minutes with each of 2X, 0.5X and 0.2X SSC containing 0.1% SDS.

It will be appreciated by those of ordinary skill in the art that, as a result of the degeneracy of the genetic code, there are many nucleotide sequences that encode a polypeptide as described herein. Some of these polynucleotides bear minimal homology to

the nucleotide sequence of any native gene. Nonetheless, polynucleotides that vary due to differences in codon usage are specifically contemplated by the present invention. Further, alleles of the genes comprising the polynucleotide sequences provided herein are within the scope of the present invention. Alleles are endogenous genes that are altered as a result of one or more mutations, such as deletions, additions and/or substitutions of nucleotides. The resulting mRNA and protein may, but need not, have an altered structure or function. Alleles may be identified using standard techniques (such as hybridization, amplification and/or database sequence comparison).

Polynucleotides may be prepared using any of a variety of techniques. For example, a polynucleotide may be identified, as described in more detail below, by screening a microarray of cDNAs for tumor-associated expression (i.e., expression that is at least five fold greater in a prostate tumor than in normal tissue, as determined using a representative assay provided herein). Such screens may be performed using a Synteni microarray (Palo Alto, CA) according to the manufacturer's instructions (and essentially as described by Schena et al., *Proc. Natl. Acad. Sci. USA 93*:10614-10619, 1996 and Heller et al., *Proc. Natl. Acad. Sci. USA 93*:10614-10619, polypeptides may be amplified from cDNA prepared from cells expressing the proteins described herein, such as prostate tumor cells. Such polynucleotides may be amplified via polymerase chain reaction (PCR). For this approach, sequence-specific primers may be designed based on the sequences provided herein, and may be purchased or synthesized.

An amplified portion may be used to isolate a full length gene from a suitable library (e.g., a prostate tumor cDNA library) using well known techniques. Within such techniques, a library (cDNA or genomic) is screened using one or more polynucleotide probes or primers suitable for amplification. Preferably, a library is size-selected to include larger molecules. Random primed libraries may also be preferred for identifying 5' and upstream regions of genes. Genomic libraries are preferred for obtaining introns and extending 5' sequences.

For hybridization techniques, a partial sequence may be labeled (e.g., by nick-translation or end-labeling with <sup>32</sup>P) using well known techniques. A bacterial or bacteriophage library is then screened by hybridizing filters containing denatured bacterial colonies (or lawns containing phage plaques) with the labeled probe (see Sambrook et al., Molecular Cloning: A Laboratory Manual, Cold Spring Harbor Laboratories, Cold Spring Harbor, NY, 1989). Hybridizing colonies or plaques are selected and expanded, and the DNA is isolated for further analysis. cDNA clones may be analyzed to determine the amount of additional sequence by, for example, PCR using a primer from the partial sequence and a primer from the vector. Restriction maps and partial sequences may be generated to identify one or more overlapping clones. The complete sequence may then be determined using

standard techniques, which may involve generating a series of deletion clones. The resulting overlapping sequences are then assembled into a single contiguous sequence. A full length cDNA molecule can be generated by ligating suitable fragments, using well known techniques.

Alternatively, there are numerous amplification techniques for obtaining a full length coding sequence from a partial cDNA sequence. Within such techniques, amplification is generally performed via PCR. Any of a variety of commercially available kits may be used to perform the amplification step. Primers may be designed using, for example, software well known in the art. Primers are preferably 22-30 nucleotides in length, have a GC content of at least 50% and anneal to the target sequence at temperatures of about 68°C to 72°C. The amplified region may be sequenced as described above, and overlapping sequences assembled into a contiguous sequence.

One such amplification technique is inverse PCR (see Triglia et al., Nucl. Acids Res. 16:8186, 1988), which uses restriction enzymes to generate a fragment in the known region of the gene. The fragment is then circularized by intramolecular ligation and used as a template for PCR with divergent primers derived from the known region. Within an alternative approach, sequences adjacent to a partial sequence may be retrieved by amplification with a primer to a linker sequence and a primer specific to a known region. The amplified sequences are typically subjected to a second round of amplification with the same linker primer and a second primer specific to the known region. A variation on this procedure, which employs two primers that initiate extension in opposite directions from the known sequence, is described in WO 96/38591. Another such technique is known as "rapid amplification of cDNA ends" or RACE. This technique involves the use of an internal primer and an external primer, which hybridizes to a polyA region or vector sequence, to identify sequences that are 5' and 3' of a known sequence. Additional techniques include capture PCR (Lagerstrom et al., PCR Methods Applic. 1:111-19, 1991) and walking PCR (Parker et al., Nucl. Acids. Res. 19:3055-60, 1991). Other methods employing amplification may also be employed to obtain a full length cDNA sequence.

In certain instances, it is possible to obtain a full length cDNA sequence by analysis of sequences provided in an expressed sequence tag (EST) database, such as that available from GenBank. Searches for overlapping ESTs may generally be performed using well known programs (e.g., NCBI BLAST searches), and such ESTs may be used to generate a contiguous full length sequence.

Certain nucleic acid sequences of cDNA molecules encoding at least a portion of a prostate tumor protein are provided in SEQ ID NOs:1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382 or 384-472. Isolation of these

polynucleotides is described below. Each of these prostate tumor proteins was overexpressed in prostate tumor tissue.

Polynucleotide variants may generally be prepared by any method known in the art, including chemical synthesis by, for example, solid phase phosphoramidite chemical synthesis. Modifications in a polynucleotide sequence may also be introduced using standard mutagenesis techniques, such as oligonucleotide-directed site-specific mutagenesis (see Adelman et al., DNA 2:183, 1983). Alternatively, RNA molecules may be generated by in vitro or in vivo transcription of DNA sequences encoding a prostate tumor protein, or portion thereof, provided that the DNA is incorporated into a vector with a suitable RNA polymerase promoter (such as T7 or SP6). Certain portions may be used to prepare an encoded polypeptide, as described herein. In addition, or alternatively, a portion may be administered to a patient such that the encoded polypeptide is generated in vivo (e.g., by transfecting antigen-presenting cells, such as dendritic cells, with a cDNA construct encoding a prostate tumor polypeptide, and administering the transfected cells to the patient).

A portion of a sequence complementary to a coding sequence (i.e., an antisense polynucleotide) may also be used as a probe or to modulate gene expression. cDNA constructs that can be transcribed into antisense RNA may also be introduced into cells of tissues to facilitate the production of antisense RNA. An antisense polynucleotide may be used, as described herein, to inhibit expression of a tumor protein. Antisense technology can be used to control gene expression through triple-helix formation, which compromises the ability of the double helix to open sufficiently for the binding of polymerases, transcription factors or regulatory molecules (see Gee et al., In Huber and Carr, Molecular and Immunologic Approaches, Futura Publishing Co. (Mt. Kisco, NY; 1994)). Alternatively, an antisense molecule may be designed to hybridize with a control region of a gene (e.g., promoter, enhancer or transcription initiation site), and block transcription of the gene; or to block translation by inhibiting binding of a transcript to ribosomes.

A portion of a coding sequence, or of a complementary sequence, may also be designed as a probe or primer to detect gene expression. Probes may be labeled with a variety of reporter groups, such as radionuclides and enzymes, and are preferably at least 10 nucleotides in length, more preferably at least 20 nucleotides in length and still more preferably at least 30 nucleotides in length. Primers, as noted above, are preferably 22-30 nucleotides in length.

Any polynucleotide may be further modified to increase stability in vivo. Possible modifications include, but are not limited to, the addition of flanking sequences at the 5' and/or 3' ends; the use of phosphorothioate or 2' O-methyl rather than phosphodiesterase linkages in the backbone; and/or the inclusion of nontraditional bases such

as inosine, queosine and wybutosine, as well as acetyl- methyl-, thio- and other modified forms of adenine, cytidine, guanine, thymine and uridine.

Nucleotide sequences as described herein may be joined to a variety of other nucleotide sequences using established recombinant DNA techniques. For example, a polynucleotide may be cloned into any of a variety of cloning vectors, including plasmids, phagemids, lambda phage derivatives and cosmids. Vectors of particular interest include expression vectors, replication vectors, probe generation vectors and sequencing vectors. In general, a vector will contain an origin of replication functional in at least one organism, convenient restriction endonuclease sites and one or more selectable markers. Other elements will depend upon the desired use, and will be apparent to those of ordinary skill in the art.

Within certain embodiments, polynucleotides may be formulated so as to permit entry into a cell of a mammal, and expression therein. Such formulations are particularly useful for therapeutic purposes, as described below. Those of ordinary skill in the art will appreciate that there are many ways to achieve expression of a polynucleotide in a target cell, and any suitable method may be employed. For example, a polynucleotide may be incorporated into a viral vector such as, but not limited to, adenovirus, adeno-associated virus, retrovirus, or vaccinia or other pox virus (e.g., avian pox virus). Techniques for incorporating DNA into such vectors are well known to those of ordinary skill in the art. A retroviral vector may additionally transfer or incorporate a gene for a selectable marker (to aid in the identification or selection of transduced cells) and/or a targeting moiety, such as a gene that encodes a ligand for a receptor on a specific target cell, to render the vector target specific. Targeting may also be accomplished using an antibody, by methods known to those of ordinary skill in the art.

Other formulations for therapeutic purposes include colloidal dispersion systems, such as macromolecule complexes, nanocapsules, microspheres, beads, and lipid-based systems including oil-in-water emulsions, micelles, mixed micelles, and liposomes. A preferred colloidal system for use as a delivery vehicle *in vitro* and *in vivo* is a liposome (*i.e.*, an artificial membrane vesicle). The preparation and use of such systems is well known in the art.

## PROSTATE TUMOR POLYPEPTIDES

Within the context of the present invention, polypeptides may comprise at least an immunogenic portion of a prostate tumor protein or a variant thereof, as described herein. As noted above, a "prostate tumor protein" is a protein that is expressed by prostate tumor cells. Proteins that are prostate tumor proteins also react detectably within an immunoassay (such as an ELISA) with antisera from a patient with prostate cancer. Polypeptides as described herein may be of any length. Additional sequences derived from

the native protein and/or heterologous sequences may be present, and such sequences may (but need not) possess further immunogenic or antigenic properties.

An "immunogenic portion," as used herein is a portion of a protein that is recognized (i.e., specifically bound) by a B-cell and/or T-cell surface antigen receptor. Such immunogenic portions generally comprise at least 5 amino acid residues, more preferably at least 10, and still more preferably at least 20 amino acid residues of a prostate tumor protein or a variant thereof. Certain preferred immunogenic portions include peptides in which an N-terminal leader sequence and/or transmembrane domain have been deleted. Other preferred immunogenic portions may contain a small N- and/or C-terminal deletion (e.g., 1-30 amino acids, preferably 5-15 amino acids), relative to the mature protein.

Immunogenic portions may generally be identified using well known techniques, such as those summarized in Paul, Fundamental Immunology, 3rd ed., 243-247 (Raven Press, 1993) and references cited therein. Such techniques include screening polypeptides for the ability to react with antigen-specific antibodies, antisera and/or T-cell lines or clones. As used herein, antisera and antibodies are "antigen-specific" if they specifically bind to an antigen (i.e., they react with the protein in an ELISA or other immunoassay, and do not react detectably with unrelated proteins). Such antisera and antibodies may be prepared as described herein, and using well known techniques. An immunogenic portion of a native prostate tumor protein is a portion that reacts with such antisera and/or T-cells at a level that is not substantially less than the reactivity of the full length polypeptide (e.g., in an ELISA and/or T-cell reactivity assay). Such immunogenic portions may react within such assays at a level that is similar to or greater than the reactivity of the full length polypeptide. Such screens may generally be performed using methods well known to those of ordinary skill in the art, such as those described in Harlow and Lane, Antibodies: A Laboratory Manual, Cold Spring Harbor Laboratory, 1988. For example, a polypeptide may be immobilized on a solid support and contacted with patient sera to allow binding of antibodies within the sera to the immobilized polypeptide. Unbound sera may then be removed and bound antibodies detected using, for example, 125I-labeled Protein A.

As noted above, a composition may comprise a variant of a native prostate tumor protein. A polypeptide "variant," as used herein, is a polypeptide that differs from a native prostate tumor protein in one or more substitutions, deletions, additions and/or insertions, such that the immunogenicity of the polypeptide is not substantially diminished. In other words, the ability of a variant to react with antigen-specific antisera may be enhanced or unchanged, relative to the native protein, or may be diminished by less than 50%, and preferably less than 20%, relative to the native protein. Such variants may generally be identified by modifying one of the above polypeptide sequences and evaluating the reactivity of the modified polypeptide with antigen-specific antibodies or antisera as described herein.

Preferred variants include those in which one or more portions, such as an N-terminal leader sequence or transmembrane domain, have been removed. Other preferred variants include variants in which a small portion (e.g., 1-30 amino acids, preferably 5-15 amino acids) has been removed from the N- and/or C-terminal of the mature protein. Polypeptide variants preferably exhibit at least about 70%, more preferably at least about 90% and most preferably at least about 95% identity (determined as described above) to the identified polypeptides.

Preferably, a variant contains conservative substitutions. A "conservative substitution" is one in which an amino acid is substituted for another amino acid that has similar properties, such that one skilled in the art of peptide chemistry would expect the secondary structure and hydropathic nature of the polypeptide to be substantially unchanged. Amino acid substitutions may generally be made on the basis of similarity in polarity, charge, solubility, hydrophobicity, hydrophilicity and/or the amphipathic nature of the residues. For example, negatively charged amino acids include aspartic acid and glutamic acid; positively charged amino acids include lysine and arginine; and amino acids with uncharged polar head groups having similar hydrophilicity values include leucine, isoleucine and valine; glycine and alanine; asparagine and glutamine; and serine, threonine, phenylalanine and tyrosine. Other groups of amino acids that may represent conservative changes include: (1) ala, pro. gly, glu, asp, gln, asn, ser, thr; (2) cys, ser, tyr, thr; (3) val, ile, leu, met, ala, phe; (4) lys, arg, his; and (5) phe, tyr, trp, his. A variant may also, or alternatively, contain nonconservative changes. In a preferred embodiment, variant polypeptides differ from a native sequence by substitution, deletion or addition of five amino acids or fewer. Variants may also (or alternatively) be modified by, for example, the deletion or addition of amino acids that have minimal influence on the immunogenicity, secondary structure and hydropathic nature of the polypeptide.

As noted above, polypeptides may comprise a signal (or leader) sequence at the N-terminal end of the protein which co-translationally or post-translationally directs transfer of the protein. The polypeptide may also be conjugated to a linker or other sequence for ease of synthesis, purification or identification of the polypeptide (e.g., poly-His), or to enhance binding of the polypeptide to a solid support. For example, a polypeptide may be conjugated to an immunoglobulin Fc region.

Polypeptides may be prepared using any of a variety of well known techniques. Recombinant polypeptides encoded by DNA sequences as described above may be readily prepared from the DNA sequences using any of a variety of expression vectors known to those of ordinary skill in the art. Expression may be achieved in any appropriate host cell that has been transformed or transfected with an expression vector containing a DNA molecule that encodes a recombinant polypeptide. Suitable host cells include prokaryotes, yeast and higher eukaryotic cells. Preferably, the host cells employed are

E. coli, yeast or a mammalian cell line such as COS or CHO. Supernatants from suitable host/vector systems which secrete recombinant protein or polypeptide into culture media may be first concentrated using a commercially available filter. Following concentration, the concentrate may be applied to a suitable purification matrix such as an affinity matrix or an ion exchange resin. Finally, one or more reverse phase HPLC steps can be employed to further purify a recombinant polypeptide.

Portions and other variants having fewer than about 100 amino acids, and generally fewer than about 50 amino acids, may also be generated by synthetic means, using techniques well known to those of ordinary skill in the art. For example, such polypeptides may be synthesized using any of the commercially available solid-phase techniques, such as the Merrifield solid-phase synthesis method, where amino acids are sequentially added to a growing amino acid chain. See Merrifield, J. Am. Chem. Soc. 85:2149-2146, 1963. Equipment for automated synthesis of polypeptides is commercially available from suppliers such as Perkin Elmer/Applied BioSystems Division (Foster City, CA), and may be operated according to the manufacturer's instructions.

Within certain specific embodiments, a polypeptide may be a fusion protein that comprises multiple polypeptides as described herein, or that comprises at least one polypeptide as described herein and an unrelated sequence, such as a known tumor protein. A fusion partner may, for example, assist in providing T helper epitopes (an immunological fusion partner), preferably T helper epitopes recognized by humans, or may assist in expressing the protein (an expression enhancer) at higher yields than the native recombinant protein. Certain preferred fusion partners are both immunological and expression enhancing fusion partners. Other fusion partners may be selected so as to increase the solubility of the protein or to enable the protein to be targeted to desired intracellular compartments. Still further fusion partners include affinity tags, which facilitate purification of the protein.

Fusion proteins may generally be prepared using standard techniques, including chemical conjugation. Preferably, a fusion protein is expressed as a recombinant protein, allowing the production of increased levels, relative to a non-fused protein, in an expression system. Briefly, DNA sequences encoding the polypeptide components may be assembled separately, and ligated into an appropriate expression vector. The 3' end of the DNA sequence encoding one polypeptide component is ligated, with or without a peptide linker, to the 5' end of a DNA sequence encoding the second polypeptide component so that the reading frames of the sequences are in phase. This permits translation into a single fusion protein that retains the biological activity of both component polypeptides.

A peptide linker sequence may be employed to separate the first and the second polypeptide components by a distance sufficient to ensure that each polypeptide folds into its secondary and tertiary structures. Such a peptide linker sequence is incorporated into

the fusion protein using standard techniques well known in the art. Suitable peptide linker sequences may be chosen based on the following factors: (1) their ability to adopt a flexible extended conformation; (2) their inability to adopt a secondary structure that could interact with functional epitopes on the first and second polypeptides; and (3) the lack of hydrophobic or charged residues that might react with the polypeptide functional epitopes. Preferred peptide linker sequences contain Gly, Asn and Ser residues. Other near neutral amino acids, such as Thr and Ala may also be used in the linker sequence. Amino acid sequences which may be usefully employed as linkers include those disclosed in Maratea et al., Gene 40:39-46, 1985; Murphy et al., Proc. Natl. Acad. Sci. USA 83:8258-8262, 1986; U.S. Patent No. 4,935,233 and U.S. Patent No. 4,751,180. The linker sequence may generally be from 1 to about 50 amino acids in length. Linker sequences are not required when the first and second polypeptides have non-essential N-terminal amino acid regions that can be used to separate the functional domains and prevent steric interference.

The ligated DNA sequences are operably linked to suitable transcriptional or translational regulatory elements. The regulatory elements responsible for expression of DNA are located only 5' to the DNA sequence encoding the first polypeptides. Similarly, stop codons required to end translation and transcription termination signals are only present 3' to the DNA sequence encoding the second polypeptide.

Fusion proteins are also provided that comprise a polypeptide of the present invention together with an unrelated immunogenic protein. Preferably the immunogenic protein is capable of eliciting a recall response. Examples of such proteins include tetanus, tuberculosis and hepatitis proteins (see, for example, Stoute et al. New Engl. J. Med., 336:86-91, 1997).

Within preferred embodiments, an immunological fusion partner is derived from protein D, a surface protein of the gram-negative bacterium Haemophilus influenza B (WO 91/18926). Preferably, a protein D derivative comprises approximately the first third of the protein (e.g., the first N-terminal 100-110 amino acids), and a protein D derivative may be lipidated. Within certain preferred embodiments, the first 109 residues of a Lipoprotein D fusion partner is included on the N-terminus to provide the polypeptide with additional exogenous T-cell epitopes and to increase the expression level in E. coli (thus functioning as an expression enhancer). The lipid tail ensures optimal presentation of the antigen to antigen presenting cells. Other fusion partners include the non-structural protein from influenzae virus, NS1 (hemaglutinin). Typically, the N-terminal 81 amino acids are used, although different fragments that include T-helper epitopes may be used.

In another embodiment, the immunological fusion partner is the protein known as LYTA, or a portion thereof (preferably a C-terminal portion). LYTA is derived from Streptococcus pneumoniae, which synthesizes an N-acetyl-L-alanine amidase known as

amidase LYTA (encoded by the LytA gene; Gene 43:265-292, 1986). LYTA is an autolysin that specifically degrades certain bonds in the peptidoglycan backbone. The C-terminal domain of the LYTA protein is responsible for the affinity to the choline or to some choline analogues such as DEAE. This property has been exploited for the development of E. coli C-LYTA expressing plasmids useful for expression of fusion proteins. Purification of hybrid proteins containing the C-LYTA fragment at the amino terminus has been described (see Biotechnology 10:795-798, 1992). Within a preferred embodiment, a repeat portion of LYTA may be incorporated into a fusion protein. A repeat portion is found in the C-terminal region starting at residue 178. A particularly preferred repeat portion incorporates residues 188-305.

In general, polypeptides (including fusion proteins) and polynucleotides as described herein are isolated. An "isolated" polypeptide or polynucleotide is one that is removed from its original environment. For example, a naturally-occurring protein is isolated if it is separated from some or all of the coexisting materials in the natural system. Preferably, such polypeptides are at least about 90% pure, more preferably at least about 95% pure and most preferably at least about 99% pure. A polynucleotide is considered to be isolated if, for example, it is cloned into a vector that is not a part of the natural environment.

### **BINDING AGENTS**

The present invention further provides agents, such as antibodies and antigen-binding fragments thereof, that specifically bind to a prostate tumor protein. As used herein, an antibody, or antigen-binding fragment thereof, is said to "specifically bind" to a prostate tumor protein if it reacts at a detectable level (within, for example, an ELISA) with a prostate tumor protein, and does not react detectably with unrelated proteins under similar conditions. As used herein, "binding" refers to a noncovalent association between two separate molecules such that a complex is formed. The ability to bind may be evaluated by, for example, determining a binding constant for the formation of the complex. The binding constant is the value obtained when the concentration of the complex is divided by the product of the component concentrations. In general, two compounds are said to "bind," in the context of the present invention, when the binding constant for complex formation exceeds about 10<sup>3</sup> L/mol. The binding constant may be determined using methods well known in the art.

Binding agents may be further capable of differentiating between patients with and without a cancer, such as prostate cancer, using the representative assays provided herein. In other words, antibodies or other binding agents that bind to a prostate tumor protein will generate a signal indicating the presence of a cancer in at least about 20% of patients with the disease, and will generate a negative signal indicating the absence of the disease in at least about 90% of individuals without the cancer. To determine whether a binding agent satisfies this requirement, biological samples (e.g., blood, sera, urine and/or tumor biopsies) from

patients with and without a cancer (as determined using standard clinical tests) may be assayed as described herein for the presence of polypeptides that bind to the binding agent. It will be apparent that a statistically significant number of samples with and without the disease should be assayed. Each binding agent should satisfy the above criteria; however, those of ordinary skill in the art will recognize that binding agents may be used in combination to improve sensitivity.

Any agent that satisfies the above requirements may be a binding agent. For example, a binding agent may be a ribosome, with or without a peptide component, an RNA molecule or a polypeptide. In a preferred embodiment, a binding agent is an antibody or an antigen-binding fragment thereof. Antibodies may be prepared by any of a variety of techniques known to those of ordinary skill in the art. See, e.g., Harlow and Lane, Antibodies: A Laboratory Manual, Cold Spring Harbor Laboratory, 1988. In general, antibodies can be produced by cell culture techniques, including the generation of monoclonal antibodies as described herein, or via transfection of antibody genes into suitable bacterial or mammalian cell hosts, in order to allow for the production of recombinant antibodies. In one technique, an immunogen comprising the polypeptide is initially injected into any of a wide variety of mammals (e.g., mice, rats, rabbits, sheep or goats). In this step, the polypeptides of this invention may serve as the immunogen without modification. Alternatively, particularly for relatively short polypeptides, a superior immune response may be elicited if the polypeptide is joined to a carrier protein, such as bovine serum albumin or keyhole limpet hemocyanin. The immunogen is injected into the animal host, preferably according to a predetermined schedule incorporating one or more booster immunizations, and the animals are bled periodically. Polyclonal antibodies specific for the polypeptide may then be purified from such antisera by, for example, affinity chromatography using the polypeptide coupled to a suitable solid support.

Monoclonal antibodies specific for an antigenic polypeptide of interest may be prepared, for example, using the technique of Kohler and Milstein, Eur. J. Immunol. 6:511-519, 1976, and improvements thereto. Briefly, these methods involve the preparation of immortal cell lines capable of producing antibodies having the desired specificity (i.e., reactivity with the polypeptide of interest). Such cell lines may be produced, for example, from spleen cells obtained from an animal immunized as described above. The spleen cells are then immortalized by, for example, fusion with a myeloma cell fusion partner, preferably one that is syngeneic with the immunized animal. A variety of fusion techniques may be employed. For example, the spleen cells and myeloma cells may be combined with a nonionic detergent for a few minutes and then plated at low density on a selective medium that supports the growth of hybrid cells, but not myeloma cells. A preferred selection technique uses HAT (hypoxanthine, aminopterin, thymidine) selection. After a sufficient

time, usually about 1 to 2 weeks, colonies of hybrids are observed. Single colonies are selected and their culture supernatants tested for binding activity against the polypeptide. Hybridomas having high reactivity and specificity are preferred.

Monoclonal antibodies may be isolated from the supernatants of growing hybridoma colonies. In addition, various techniques may be employed to enhance the yield, such as injection of the hybridoma cell line into the peritoneal cavity of a suitable vertebrate host, such as a mouse. Monoclonal antibodies may then be harvested from the ascites fluid or the blood. Contaminants may be removed from the antibodies by conventional techniques, such as chromatography, gel filtration, precipitation, and extraction. The polypeptides of this invention may be used in the purification process in, for example, an affinity chromatography step.

Within certain embodiments, the use of antigen-binding fragments of antibodies may be preferred. Such fragments include Fab fragments, which may be prepared using standard techniques. Briefly, immunoglobulins may be purified from rabbit serum by affinity chromatography on Protein A bead columns (Harlow and Lane, Antibodies: A Laboratory Manual, Cold Spring Harbor Laboratory, 1988) and digested by papain to yield Fab and Fc fragments. The Fab and Fc fragments may be separated by affinity chromatography on protein A bead columns.

Monoclonal antibodies of the present invention may be coupled to one or more therapeutic agents. Suitable agents in this regard include radionuclides, differentiation inducers, drugs, toxins, and derivatives thereof. Preferred radionuclides include <sup>90</sup>Y, <sup>123</sup>I, <sup>125</sup>I, <sup>131</sup>I, <sup>186</sup>Re, <sup>188</sup>Re, <sup>211</sup>At, and <sup>212</sup>Bi. Preferred drugs include methotrexate, and pyrimidine and purine analogs. Preferred differentiation inducers include phorbol esters and butyric acid. Preferred toxins include ricin, abrin, diptheria toxin, cholera toxin, gelonin, Pseudomonas exotoxin, Shigella toxin, and pokeweed antiviral protein.

A therapeutic agent may be coupled (e.g., covalently bonded) to a suitable monoclonal antibody either directly or indirectly (e.g., via a linker group). A direct reaction between an agent and an antibody is possible when each possesses a substituent capable of reacting with the other. For example, a nucleophilic group, such as an amino or sulfhydryl group, on one may be capable of reacting with a carbonyl-containing group, such as an anhydride or an acid halide, or with an alkyl group containing a good leaving group (e.g., a halide) on the other.

Alternatively, it may be desirable to couple a therapeutic agent and an antibody via a linker group. A linker group can function as a spacer to distance an antibody from an agent in order to avoid interference with binding capabilities. A linker group can also serve to increase the chemical reactivity of a substituent on an agent or an antibody, and

thus increase the coupling efficiency. An increase in chemical reactivity may also facilitate the use of agents, or functional groups on agents, which otherwise would not be possible.

It will be evident to those skilled in the art that a variety of bifunctional or polyfunctional reagents, both homo- and hetero-functional (such as those described in the catalog of the Pierce Chemical Co., Rockford, IL), may be employed as the linker group. Coupling may be effected, for example, through amino groups, carboxyl groups, sulfhydryl groups or oxidized carbohydrate residues. There are numerous references describing such methodology, e.g., U.S. Patent No. 4,671,958, to Rodwell et al.

Where a therapeutic agent is more potent when free from the antibody portion of the immunoconjugates of the present invention, it may be desirable to use a linker group which is cleavable during or upon internalization into a cell. A number of different cleavable linker groups have been described. The mechanisms for the intracellular release of an agent from these linker groups include cleavage by reduction of a disulfide bond (e.g., U.S. Patent No. 4,489,710, to Spitler), by irradiation of a photolabile bond (e.g., U.S. Patent No. 4,625,014, to Senter et al.), by hydrolysis of derivatized amino acid side chains (e.g., U.S. Patent No. 4,638,045, to Kohn et al.), by serum complement-mediated hydrolysis (e.g., U.S. Patent No. 4,671,958, to Rodwell et al.), and acid-catalyzed hydrolysis (e.g., U.S. Patent No. 4,569,789, to Blattler et al.).

It may be desirable to couple more than one agent to an antibody. In one embodiment, multiple molecules of an agent are coupled to one antibody molecule. In another embodiment, more than one type of agent may be coupled to one antibody. Regardless of the particular embodiment, immunoconjugates with more than one agent may be prepared in a variety of ways. For example, more than one agent may be coupled directly to an antibody molecule, or linkers which provide multiple sites for attachment can be used. Alternatively, a carrier can be used.

A carrier may bear the agents in a variety of ways, including covalent bonding either directly or via a linker group. Suitable carriers include proteins such as albumins (e.g., U.S. Patent No. 4,507,234, to Kato et al.), peptides and polysaccharides such as aminodextran (e.g., U.S. Patent No. 4,699,784, to Shih et al.). A carrier may also bear an agent by noncovalent bonding or by encapsulation, such as within a liposome vesicle (e.g., U.S. Patent Nos. 4,429,008 and 4,873,088). Carriers specific for radionuclide agents include radiohalogenated small molecules and chelating compounds. For example, U.S. Patent No. 4,735,792 discloses representative radiohalogenated small molecules and their synthesis. A radionuclide chelate may be formed from chelating compounds that include those containing nitrogen and sulfur atoms as the donor atoms for binding the metal, or metal oxide, radionuclide. For example, U.S. Patent No. 4,673,562, to Davison et al. discloses representative chelating compounds and their synthesis.

A variety of routes of administration for the antibodies and immunoconjugates may be used. Typically, administration will be intravenous, intramuscular, subcutaneous or in the bed of a resected tumor. It will be evident that the precise dose of the antibody/immunoconjugate will vary depending upon the antibody used, the antigen density on the tumor, and the rate of clearance of the antibody.

#### T CELLS

Immunotherapeutic compositions may also, or alternatively, comprise T cells specific for a prostate tumor protein. Such cells may generally be prepared *in vitro* or *ex vivo*, using standard procedures. For example, T cells may be isolated from bone marrow, peripheral blood, or a fraction of bone marrow or peripheral blood of a patient, using a commercially available cell separation system, such as the CEPRATE<sup>TM</sup> system, available from CellPro Inc., Bothell WA (*see also* U.S. Patent No. 5,240,856; U.S. Patent No. 5,215,926; WO 89/06280; WO 91/16116 and WO 92/07243). Alternatively, T cells may be derived from related or unrelated humans, non-human mammals, cell lines or cultures.

T cells may be stimulated with a prostate tumor polypeptide, polynucleotide encoding a prostate tumor polypeptide and/or an antigen presenting cell (APC) that expresses such a polypeptide. Such stimulation is performed under conditions and for a time sufficient to permit the generation of T cells that are specific for the polypeptide. Preferably, a prostate tumor polypeptide or polynucleotide is present within a delivery vehicle, such as a microsphere, to facilitate the generation of specific T cells.

T cells are considered to be specific for a prostate tumor polypeptide if the T cells kill target cells coated with the polypeptide or expressing a gene encoding the polypeptide. T cell specificity may be evaluated using any of a variety of standard For example, within a chromium release assay or proliferation assay, a techniques. stimulation index of more than two fold increase in lysis and/or proliferation, compared to negative controls, indicates T cell specificity. Such assays may be performed, for example, as described in Chen et al., Cancer Res. 54:1065-1070, 1994. Alternatively, detection of the proliferation of T cells may be accomplished by a variety of known techniques. For example, T cell proliferation can be detected by measuring an increased rate of DNA synthesis (e.g., by pulse-labeling cultures of T cells with tritiated thymidine and measuring the amount of tritiated thymidine incorporated into DNA). Contact with a prostate tumor polypeptide (100 ng/ml - 100 µg/ml, preferably 200 ng/ml - 25 µg/ml) for 3 - 7 days should result in at least a two fold increase in proliferation of the T cells. Contact as described above for 2-3 hours should result in activation of the T cells, as measured using standard cytokine assays in which a two fold increase in the level of cytokine release (e.g., TNF or IFN-γ) is indicative of T cell activation (see Coligan et al., Current Protocols in Immunology, vol. 1, Wiley Interscience

(Greene 1998)). T cells that have been activated in response to a prostate tumor polypeptide, polynucleotide or polypeptide-expressing APC may be CD4<sup>+</sup> and/or CD8<sup>+</sup>. Prostate tumor protein-specific T cells may be expanded using standard techniques. Within preferred embodiments, the T cells are derived from either a patient or a related, or unrelated, donor and are administered to the patient following stimulation and expansion.

For therapeutic purposes, CD4<sup>+</sup> or CD8<sup>+</sup> T cells that proliferate in response to a prostate tumor polypeptide, polynucleotide or APC can be expanded in number either in vitro or in vivo. Proliferation of such T cells in vitro may be accomplished in a variety of ways. For example, the T cells can be re-exposed to a prostate tumor polypeptide, or a short peptide corresponding to an immunogenic portion of such a polypeptide, with or without the addition of T cell growth factors, such as interleukin-2, and/or stimulator cells that synthesize a prostate tumor polypeptide. Alternatively, one or more T cells that proliferate in the presence of a prostate tumor protein can be expanded in number by cloning. Methods for cloning cells are well known in the art, and include limiting dilution.

## PHARMACEUTICAL COMPOSITIONS AND VACCINES

Within certain aspects, polypeptides, polynucleotides, T cells and/or binding agents disclosed herein may be incorporated into pharmaceutical compositions or immunogenic compositions (i.e., vaccines). Pharmaceutical compositions comprise one or more such compounds and a physiologically acceptable carrier. Vaccines may comprise one or more such compounds and a non-specific immune response enhancer. A non-specific immune response enhancer may be any substance that enhances an immune response to an exogenous antigen. Examples of non-specific immune response enhancers include adjuvants, biodegradable microspheres (e.g., polylactic galactide) and liposomes (into which the compound is incorporated; see e.g., Fullerton, U.S. Patent No. 4,235,877). Vaccine preparation is generally described in, for example, M.F. Powell and M.J. Newman, eds., "Vaccine Design (the subunit and adjuvant approach)," Plenum Press (NY, 1995). Pharmaceutical compositions and vaccines within the scope of the present invention may also contain other compounds, which may be biologically active or inactive. For example, one or more immunogenic portions of other tumor antigens may be present, either incorporated into a fusion polypeptide or as a separate compound, within the composition or vaccine.

A pharmaceutical composition or vaccine may contain DNA encoding one or more of the polypeptides as described above, such that the polypeptide is generated *in situ*. As noted above, the DNA may be present within any of a variety of delivery systems known to those of ordinary skill in the art, including nucleic acid expression systems, bacteria and viral expression systems. Numerous gene delivery techniques are well known in the art, such as those described by Rolland, *Crit. Rev. Therap. Drug Carrier Systems* 15:143-198, 1998,

and references cited therein. Appropriate nucleic acid expression systems contain the necessary DNA sequences for expression in the patient (such as a suitable promoter and terminating signal). Bacterial delivery systems involve the administration of a bacterium -(such as Bacillus-Calmette-Guerrin) that expresses an immunogenic portion of the polypeptide on its cell surface or secretes such an epitope. In a preferred embodiment, the DNA may be introduced using a viral expression system (e.g., vaccinia or other pox virus, retrovirus, or adenovirus), which may involve the use of a non-pathogenic (defective), replication competent virus. Suitable systems are disclosed, for example, in Fisher-Hoch et al., Proc. Natl. Acad. Sci. USA 86:317-321, 1989; Flexner et al., Ann. N.Y. Acad. Sci. 569:86-103, 1989; Flexner et al., Vaccine 8:17-21, 1990; U.S. Patent Nos. 4,603,112, 4,769,330, and 5,017,487; WO 89/01973; U.S. Patent No. 4,777,127; GB 2,200,651; EP 0,345,242; WO 91/02805; Berkner, Biotechniques 6:616-627, 1988; Rosenfeld et al., Science 252:431-434, 1991; Kolls et al., Proc. Natl. Acad. Sci. USA 91:215-219, 1994; Kass-Eisler et al., Proc. Natl. Acad. Sci. USA 90:11498-11502, 1993; Guzman et al., Circulation 88:2838-2848, 1993; and Guzman et al., Cir. Res. 73:1202-1207, 1993. Techniques for incorporating DNA into such expression systems are well known to those of ordinary skill in the art. The DNA may also be "naked," as described, for example, in Ulmer et al., Science 259:1745-1749, 1993 and reviewed by Cohen, Science 259:1691-1692, 1993. The uptake of naked DNA may be increased by coating the DNA onto biodegradable beads, which are efficiently transported into the cells.

While any suitable carrier known to those of ordinary skill in the art may be employed in the pharmaceutical compositions of this invention, the type of carrier will vary depending on the mode of administration. Compositions of the present invention may be formulated for any appropriate manner of administration, including for example, topical, oral, nasal, intravenous, intracranial, intraperitoneal, subcutaneous or intramuscular administration. For parenteral administration, such as subcutaneous injection, the carrier preferably comprises water, saline, alcohol, a fat, a wax or a buffer. For oral administration, any of the above carriers or a solid carrier, such as mannitol, lactose, starch, magnesium stearate, sodium saccharine, talcum, cellulose, glucose, sucrose, and magnesium carbonate, may be employed. Biodegradable microspheres (e.g., polylactate polyglycolate) may also be employed as carriers for the pharmaceutical compositions of this invention. Suitable biodegradable microspheres are disclosed, for example, in U.S. Patent Nos. 4,897,268 and 5,075,109.

Such compositions may also comprise buffers (e.g., neutral buffered saline or phosphate buffered saline), carbohydrates (e.g., glucose, mannose, sucrose or dextrans), mannitol, proteins, polypeptides or amino acids such as glycine, antioxidants, chelating agents such as EDTA or glutathione, adjuvants (e.g., aluminum hydroxide) and/or

preservatives. Alternatively, compositions of the present invention may be formulated as a lyophilizate. Compounds may also be encapsulated within liposomes using well known technology.

Any of a variety of non-specific immune response enhancers may be employed in the vaccines of this invention. For example, an adjuvant may be included. Most adjuvants contain a substance designed to protect the antigen from rapid catabolism, such as aluminum hydroxide or mineral oil, and a stimulator of immune responses, such as lipid A, Bortadella pertussis or Mycobacterium tuberculosis derived proteins. Suitable adjuvants are commercially available as, for example, Freund's Incomplete Adjuvant and Complete Adjuvant (Difco Laboratories, Detroit, MI); Merck Adjuvant 65 (Merck and Company, Inc., Rahway, NJ); aluminum salts such as aluminum hydroxide gel (alum) or aluminum phosphate; salts of calcium, iron or zinc; an insoluble suspension of acylated tyrosine; acylated sugars; cationically or anionically derivatized polysaccharides; polyphosphazenes; biodegradable microspheres; monophosphoryl lipid A and quil A. Cytokines, such as GM-CSF or interleukin-2, -7, or -12, may also be used as adjuvants.

Within the vaccines provided herein, the adjuvant composition is preferably designed to induce an immune response predominantly of the Th1 type. High levels of Th1-type cytokines (e.g., IFN-γ, IL-2 and IL-12) tend to favor the induction of cell mediated immune responses to an administered antigen. In contrast, high levels of Th2-type cytokines (e.g., IL-4, IL-5, IL-6, IL-10 and TNF-β) tend to favor the induction of humoral immune responses. Following application of a vaccine as provided herein, a patient will support an immune response that includes Th1- and Th2-type responses. Within a preferred embodiment, in which a response is predominantly Th1-type, the level of Th1-type cytokines will increase to a greater extent than the level of Th2-type cytokines. The levels of these cytokines may be readily assessed using standard assays. For a review of the families of cytokines, see Mosmann and Coffman, Ann. Rev. Immunol. 7:145-173, 1989.

Preferred adjuvants for use in eliciting a predominantly Th1-type response include, for example, a combination of monophosphoryl lipid A, preferably 3-de-O-acylated monophosphoryl lipid A (3D-MPL), together with an aluminum salt. MPL adjuvants are available from Ribi ImmunoChem Research Inc. (Hamilton, MT; see US Patent Nos. 4,436,727; 4,877,611; 4,866,034 and 4,912,094). CpG-containing oligonucleotides (in which the CpG dinucleotide is unmethylated) also induce a predominantly Th1 response. Such oligonucleotides are well known and are described, for example, in WO 96/02555. Another preferred adjuvant is a saponin, preferably QS21, which may be used alone or in combination with other adjuvants. For example, an enhanced system involves the combination of a monophosphoryl lipid A and saponin derivative, such as the combination of QS21 and 3D-MPL as described in WO 94/00153, or a less reactogenic composition where the QS21 is

quenched with cholesterol, as described in WO 96/33739. Other preferred formulations comprises an oil-in-water emulsion and tocopherol. A particularly potent adjuvant formulation involving QS21, 3D-MPL and tocopherol in an oil-in-water emulsion is described in WO 95/17210. Any vaccine provided herein may be prepared using well known methods that result in a combination of antigen, immune response enhancer and a suitable carrier or excipient.

The compositions described herein may be administered as part of a sustained release formulation (i.e., a formulation such as a capsule or sponge that effects a slow release of compound following administration). Such formulations may generally be prepared using well known technology and administered by, for example, oral, rectal or subcutaneous implantation, or by implantation at the desired target site. Sustained-release formulations may contain a polypeptide, polynucleotide or antibody dispersed in a carrier matrix and/or contained within a reservoir surrounded by a rate controlling membrane. Carriers for use within such formulations are biocompatible, and may also be biodegradable; preferably the formulation provides a relatively constant level of active component release. The amount of active compound contained within a sustained release formulation depends upon the site of implantation, the rate and expected duration of release and the nature of the condition to be treated or prevented.

Any of a variety of delivery vehicles may be employed within pharmaceutical compositions and vaccines to facilitate production of an antigen-specific immune response that targets tumor cells. Delivery vehicles include antigen presenting cells (APCs), such as dendritic cells, macrophages, B cells, monocytes and other cells that may be engineered to be efficient APCs. Such cells may, but need not, be genetically modified to increase the capacity for presenting the antigen, to improve activation and/or maintenance of the T cell response, to have anti-tumor effects *per se* and/or to be immunologically compatible with the receiver (*i.e.*, matched HLA haplotype). APCs may generally be isolated from any of a variety of biological fluids and organs, including tumor and peritumoral tissues, and may be autologous, allogeneic, syngeneic or xenogeneic cells.

Certain preferred embodiments of the present invention use dendritic cells or progenitors thereof as antigen-presenting cells. Dendritic cells are highly potent APCs (Banchereau and Steinman, *Nature 392*:245-251, 1998) and have been shown to be effective as a physiological adjuvant for eliciting prophylactic or therapeutic antitumor immunity (*see* Timmerman and Levy, *Ann. Rev. Med. 50*:507-529, 1999). In general, dendritic cells may be identified based on their typical shape (stellate *in situ*, with marked cytoplasmic processes (dendrites) visible *in vitro*) and based on the lack of differentiation markers of B cells (CD19 and CD20), T cells (CD3), monocytes (CD14) and natural killer cells (CD56), as determined using standard assays. Dendritic cells may, of course, be engineered to express specific cell-

surface receptors or ligands that are not commonly found on dendritic cells in vivo or ex vivo, and such modified dendritic cells are contemplated by the present invention. As an alternative to dendritic cells, secreted vesicles antigen-loaded dendritic cells (called exosomes) may be used within a vaccine (see Zitvogel et al., Nature Med. 4:594-600, 1998).

Dendritic cells and progenitors may be obtained from peripheral blood, bone marrow, tumor-infiltrating cells, peritumoral tissues-infiltrating cells, lymph nodes, spleen, skin, umbilical cord blood or any other suitable tissue or fluid. For example, dendritic cells may be differentiated *ex vivo* by adding a combination of cytokines such as GM-CSF, IL-4, IL-13 and/or TNFα to cultures of monocytes harvested from peripheral blood. Alternatively, CD34 positive cells harvested from peripheral blood, umbilical cord blood or bone marrow may be differentiated into dendritic cells by adding to the culture medium combinations of GM-CSF, IL-3, TNFα, CD40 ligand, LPS, flt3 ligand and/or other compound(s) that induce maturation and proliferation of dendritic cells.

Dendritic cells are conveniently categorized as "immature" and "mature" cells, which allows a simple way to discriminate between two well characterized phenotypes. However, this nomenclature should not be construed to exclude all possible intermediate stages of differentiation. Immature dendritic cells are characterized as APC with a high capacity for antigen uptake and processing, which correlates with the high expression of Fcy receptor, mannose receptor and DEC-205 marker. The mature phenotype is typically characterized by a lower expression of these markers, but a high expression of cell surface molecules responsible for T cell activation such as class I and class II MHC, adhesion molecules (e.g., CD54 and CD11) and costimulatory molecules (e.g., CD40, CD80 and CD86).

APCs may generally be transfected with a polynucleotide encoding a prostate tumor protein (or portion or other variant thereof) such that the prostate tumor polypeptide, or an immunogenic portion thereof, is expressed on the cell surface. Such transfection may take place ex vivo, and a composition or vaccine comprising such transfected cells may then be used for therapeutic purposes, as described herein. Alternatively, a gene delivery vehicle that targets a dendritic or other antigen presenting cell may be administered to a patient, resulting in transfection that occurs in vivo. In vivo and ex vivo transfection of dendritic cells, for example, may generally be performed using any methods known in the art, such as those described in WO 97/24447, or the gene gun approach described by Mahvi et al., Immunology and cell Biology 75:456-460, 1997. Antigen loading of dendritic cells may be achieved by incubating dendritic cells or progenitor cells with the prostate tumor polypeptide, DNA (naked or within a plasmid vector) or RNA; or with antigen-expressing recombinant bacterium or viruses (e.g., vaccinia, fowlpox, adenovirus or lentivirus vectors). Prior to loading, the polypeptide may be covalently conjugated to an immunological partner that

provides T cell help (e.g., a carrier molecule). Alternatively, a dendritic cell may be pulsed with a non-conjugated immunological partner, separately or in the presence of the polypeptide.

### **CANCER THERAPY**

In further aspects of the present invention, the compositions described herein may be used for immunotherapy of cancer, such as prostate cancer. Within such methods, pharmaceutical compositions and vaccines are typically administered to a patient. As used herein, a "patient" refers to any warm-blooded animal, preferably a human. A patient may or may not be afflicted with cancer. Accordingly, the above pharmaceutical compositions and vaccines may be used to prevent the development of a cancer or to treat a patient afflicted with a cancer. A cancer may be diagnosed using criteria generally accepted in the art, including the presence of a malignant tumor. Pharmaceutical compositions and vaccines may be administered either prior to or following surgical removal of primary tumors and/or treatment such as administration of radiotherapy or conventional chemotherapeutic drugs.

Within certain embodiments, immunotherapy may be active immunotherapy, in which treatment relies on the *in vivo* stimulation of the endogenous host immune system to react against tumors with the administration of immune response-modifying agents (such as polypeptides and polynucleotides disclosed herein).

Within other embodiments, immunotherapy may be passive immunotherapy, in which treatment involves the delivery of agents with established tumor-immune reactivity (such as effector cells or antibodies) that can directly or indirectly mediate antitumor effects and does not necessarily depend on an intact host immune system. Examples of effector cells include T cells as discussed above, T lymphocytes (such as CD8+ cytotoxic T lymphocytes and CD4+ T-helper tumor-infiltrating lymphocytes), killer cells (such as Natural Killer cells and lymphokine-activated killer cells), B cells and antigen-presenting cells (such as dendritic cells and macrophages) expressing a polypeptide provided herein. T cell receptors and antibody receptors specific for the polypeptides recited herein may be cloned, expressed and transferred into other vectors or effector cells for adoptive immunotherapy. The polypeptides provided herein may also be used to generate antibodies or anti-idiotypic antibodies (as described above and in U.S. Patent No. 4,918,164) for passive immunotherapy.

Effector cells may generally be obtained in sufficient quantities for adoptive immunotherapy by growth *in vitro*, as described herein. Culture conditions for expanding single antigen-specific effector cells to several billion in number with retention of antigen recognition *in vivo* are well known in the art. Such *in vitro* culture conditions typically use intermittent stimulation with antigen, often in the presence of cytokines (such as IL-2) and non-dividing feeder cells. As noted above, immunoreactive polypeptides as provided herein

may be used to rapidly expand antigen-specific T cell cultures in order to generate a sufficient number of cells for immunotherapy. In particular, antigen-presenting cells, such as dendritic, macrophage, monocyte, fibroblast or B cells, may be pulsed with immunoreactive polypeptides or transfected with one or more polynucleotides using standard techniques well known in the art. For example, antigen-presenting cells can be transfected with a polynucleotide having a promoter appropriate for increasing expression in a recombinant virus or other expression system. Cultured effector cells for use in therapy must be able to grow and distribute widely, and to survive long term *in vivo*. Studies have shown that cultured effector cells can be induced to grow in vivo and to survive long term in substantial numbers by repeated stimulation with antigen supplemented with IL-2 (see, for example, Cheever et al., Immunological Reviews 157:177, 1997).

Alternatively, a vector expressing a polypeptide recited herein may be introduced into antigen presenting cells taken from a patient and clonally propagated ex vivo for transplant back into the same patient. Transfected cells may be reintroduced into the patient using any means known in the art, preferably in sterile form by intravenous, intracavitary, intraperitoneal or intratumor administration.

Routes and frequency of administration of the therapeutic compositions disclosed herein, as well as dosage, will vary from individual to individual, and may be readily established using standard techniques. In general, the pharmaceutical compositions and vaccines may be administered by injection (e.g., intracutaneous, intramuscular, intravenous or subcutaneous), intranasally (e.g., by aspiration) or orally. Preferably, between 1 and 10 doses may be administered over a 52 week period. Preferably, 6 doses are administered, at intervals of 1 month, and booster vaccinations may be given periodically thereafter. Alternate protocols may be appropriate for individual patients. A suitable dose is an amount of a compound that, when administered as described above, is capable of promoting an anti-tumor immune response, and is at least 10-50% above the basal (i.e., untreated) level. Such response can be monitored by measuring the anti-tumor antibodies in a patient or by vaccine-dependent generation of cytolytic effector cells capable of killing the patient's tumor cells in vitro. Such vaccines should also be capable of causing an immune response that leads to an improved clinical outcome (e.g., more frequent remissions, complete or partial or longer disease-free survival) in vaccinated patients as compared to nonvaccinated patients. In general, for pharmaceutical compositions and vaccines comprising one or more polypeptides, the amount of each polypeptide present in a dose ranges from about 100 µg to 5 mg per kg of host. Suitable dose sizes will vary with the size of the patient, but will typically range from about 0.1 mL to about 5 mL.

In general, an appropriate dosage and treatment regimen provides the active compound(s) in an amount sufficient to provide therapeutic and/or prophylactic benefit. Such

a response can be monitored by establishing an improved clinical outcome (e.g., more frequent remissions, complete or partial, or longer disease-free survival) in treated patients as compared to non-treated patients. Increases in preexisting immune responses to a prostate tumor protein generally correlate with an improved clinical outcome. Such immune responses may generally be evaluated using standard proliferation, cytotoxicity or cytokine assays, which may be performed using samples obtained from a patient before and after treatment.

### METHODS FOR DETECTING CANCER

In general, a cancer may be detected in a patient based on the presence of one or more prostate tumor proteins and/or polynucleotides encoding such proteins in a biological sample (for example, blood, sera, urine and/or tumor biopsies) obtained from the patient. In other words, such proteins may be used as markers to indicate the presence or absence of a cancer such as prostate cancer. In addition, such proteins may be useful for the detection of other cancers. The binding agents provided herein generally permit detection of the level of antigen that binds to the agent in the biological sample. Polynucleotide primers and probes may be used to detect the level of mRNA encoding a tumor protein, which is also indicative of the presence or absence of a cancer. In general, a prostate tumor sequence should be present at a level that is at least three fold higher in tumor tissue than in normal tissue

There are a variety of assay formats known to those of ordinary skill in the art for using a binding agent to detect polypeptide markers in a sample. See, e.g., Harlow and Lane, Antibodies: A Laboratory Manual, Cold Spring Harbor Laboratory, 1988. In general, the presence or absence of a cancer in a patient may be determined by (a) contacting a biological sample obtained from a patient with a binding agent; (b) detecting in the sample a level of polypeptide that binds to the binding agent; and (c) comparing the level of polypeptide with a predetermined cut-off value.

In a preferred embodiment, the assay involves the use of binding agent immobilized on a solid support to bind to and remove the polypeptide from the remainder of the sample. The bound polypeptide may then be detected using a detection reagent that contains a reporter group and specifically binds to the binding agent/polypeptide complex. Such detection reagents may comprise, for example, a binding agent that specifically binds to the polypeptide or an antibody or other agent that specifically binds to the binding agent, such as an anti-immunoglobulin, protein G, protein A or a lectin. Alternatively, a competitive assay may be utilized, in which a polypeptide is labeled with a reporter group and allowed to bind to the immobilized binding agent after incubation of the binding agent with the sample. The extent to which components of the sample inhibit the binding of the labeled polypeptide to the binding agent is indicative of the reactivity of the sample with the immobilized binding

agent. Suitable polypeptides for use within such assays include full length prostate tumor proteins and portions thereof to which the binding agent binds, as described above.

The solid support may be any material known to those of ordinary skill in the art to which the tumor protein may be attached. For example, the solid support may be a test well in a microtiter plate or a nitrocellulose or other suitable membrane. Alternatively, the support may be a bead or disc, such as glass, fiberglass, latex or a plastic material such as polystyrene or polyvinylchloride. The support may also be a magnetic particle or a fiber optic sensor, such as those disclosed, for example, in U.S. Patent No. 5,359,681. The binding agent may be immobilized on the solid support using a variety of techniques known to those of skill in the art, which are amply described in the patent and scientific literature. In the context of the present invention, the term "immobilization" refers to both noncovalent association, such as adsorption, and covalent attachment (which may be a direct linkage between the agent and functional groups on the support or may be a linkage by way of a cross-linking agent). Immobilization by adsorption to a well in a microtiter plate or to a membrane is preferred. In such cases, adsorption may be achieved by contacting the binding agent, in a suitable buffer, with the solid support for a suitable amount of time. The contact time varies with temperature, but is typically between about 1 hour and about 1 day. In general, contacting a well of a plastic microtiter plate (such as polystyrene or polyvinylchloride) with an amount of binding agent ranging from about 10 ng to about 10 µg, and preferably about 100 ng to about 1 µg, is sufficient to immobilize an adequate amount of binding agent.

Covalent attachment of binding agent to a solid support may generally be achieved by first reacting the support with a bifunctional reagent that will react with both the support and a functional group, such as a hydroxyl or amino group, on the binding agent. For example, the binding agent may be covalently attached to supports having an appropriate polymer coating using benzoquinone or by condensation of an aldehyde group on the support with an amine and an active hydrogen on the binding partner (see, e.g., Pierce Immunotechnology Catalog and Handbook, 1991, at A12-A13).

In certain embodiments, the assay is a two-antibody sandwich assay. This assay may be performed by first contacting an antibody that has been immobilized on a solid support, commonly the well of a microtiter plate, with the sample, such that polypeptides within the sample are allowed to bind to the immobilized antibody. Unbound sample is then removed from the immobilized polypeptide-antibody complexes and a detection reagent (preferably a second antibody capable of binding to a different site on the polypeptide) containing a reporter group is added. The amount of detection reagent that remains bound to the solid support is then determined using a method appropriate for the specific reporter group.

More specifically, once the antibody is immobilized on the support as described above, the remaining protein binding sites on the support are typically blocked. Any suitable blocking agent known to those of ordinary skill in the art, such as bovine serum albumin or Tween 20<sup>TM</sup> (Sigma Chemical Co., St. Louis, MO). The immobilized antibody is then incubated with the sample, and polypeptide is allowed to bind to the antibody. The sample may be diluted with a suitable diluent, such as phosphate-buffered saline (PBS) prior to incubation. In general, an appropriate contact time (i.e., incubation time) is a period of time that is sufficient to detect the presence of polypeptide within a sample obtained from an individual with prostate cancer. Preferably, the contact time is sufficient to achieve a level of binding that is at least about 95% of that achieved at equilibrium between bound and unbound polypeptide. Those of ordinary skill in the art will recognize that the time necessary to achieve equilibrium may be readily determined by assaying the level of binding that occurs over a period of time. At room temperature, an incubation time of about 30 minutes is generally sufficient.

Unbound sample may then be removed by washing the solid support with an appropriate buffer, such as PBS containing 0.1% Tween 20<sup>TM</sup>. The second antibody, which contains a reporter group, may then be added to the solid support. Preferred reporter groups include those groups recited above.

The detection reagent is then incubated with the immobilized antibody-polypeptide complex for an amount of time sufficient to detect the bound polypeptide. An appropriate amount of time may generally be determined by assaying the level of binding that occurs over a period of time. Unbound detection reagent is then removed and bound detection reagent is detected using the reporter group. The method employed for detecting the reporter group depends upon the nature of the reporter group. For radioactive groups, scintillation counting or autoradiographic methods are generally appropriate. Spectroscopic methods may be used to detect dyes, luminescent groups and fluorescent groups. Biotin may be detected using avidin, coupled to a different reporter group (commonly a radioactive or fluorescent group or an enzyme). Enzyme reporter groups may generally be detected by the addition of substrate (generally for a specific period of time), followed by spectroscopic or other analysis of the reaction products.

To determine the presence or absence of a cancer, such as prostate cancer, the signal detected from the reporter group that remains bound to the solid support is generally compared to a signal that corresponds to a predetermined cut-off value. In one preferred embodiment, the cut-off value for the detection of a cancer is the average mean signal obtained when the immobilized antibody is incubated with samples from patients without the cancer. In general, a sample generating a signal that is three standard deviations above the predetermined cut-off value is considered positive for the cancer. In an alternate preferred

embodiment, the cut-off value is determined using a Receiver Operator Curve, according to the method of Sackett et al., Clinical Epidemiology: A Basic Science for Clinical Medicine, Little Brown and Co., 1985, p. 106-7. Briefly, in this embodiment, the cut-off value may be determined from a plot of pairs of true positive rates (i.e., sensitivity) and false positive rates (100%-specificity) that correspond to each possible cut-off value for the diagnostic test result. The cut-off value on the plot that is the closest to the upper left-hand corner (i.e., the value that encloses the largest area) is the most accurate cut-off value, and a sample generating a signal that is higher than the cut-off value determined by this method may be considered positive. Alternatively, the cut-off value may be shifted to the left along the plot, to minimize the false positive rate, or to the right, to minimize the false negative rate. In general, a sample generating a signal that is higher than the cut-off value determined by this method is considered positive for a cancer.

In a related embodiment, the assay is performed in a flow-through or strip test format, wherein the binding agent is immobilized on a membrane, such as nitrocellulose. In the flow-through test, polypeptides within the sample bind to the immobilized binding agent as the sample passes through the membrane. A second, labeled binding agent then binds to the binding agent-polypeptide complex as a solution containing the second binding agent flows through the membrane. The detection of bound second binding agent may then be performed as described above. In the strip test format, one end of the membrane to which binding agent is bound is immersed in a solution containing the sample. The sample migrates along the membrane through a region containing second binding agent and to the area of immobilized binding agent. Concentration of second binding agent at the area of immobilized antibody indicates the presence of a cancer. Typically, the concentration of second binding agent at that site generates a pattern, such as a line, that can be read visually. The absence of such a pattern indicates a negative result. In general, the amount of binding agent immobilized on the membrane is selected to generate a visually discernible pattern when the biological sample contains a level of polypeptide that would be sufficient to generate a positive signal in the two-antibody sandwich assay, in the format discussed above. Preferred binding agents for use in such assays are antibodies and antigen-binding fragments thereof. Preferably, the amount of antibody immobilized on the membrane ranges from about 25 ng to about 1µg, and more preferably from about 50 ng to about 500 ng. Such tests can typically be performed with a very small amount of biological sample.

Of course, numerous other assay protocols exist that are suitable for use with the tumor proteins or binding agents of the present invention. The above descriptions are intended to be exemplary only. For example, it will be apparent to those of ordinary skill in the art that the above protocols may be readily modified to use prostate tumor polypeptides to detect antibodies that bind to such polypeptides in a biological sample. The detection of such prostate tumor protein specific antibodies may correlate with the presence of a cancer.

A cancer may also, or alternatively, be detected based on the presence of T cells that specifically react with a prostate tumor protein in a biological sample. Within certain methods, a biological sample comprising CD4<sup>+</sup> and/or CD8<sup>+</sup> T cells isolated from a patient is incubated with a prostate tumor polypeptide, a polynucleotide encoding such a polypeptide and/or an APC that expresses at least an immunogenic portion of such a polypeptide, and the presence or absence of specific activation of the T cells is detected. Suitable biological samples include, but are not limited to, isolated T cells. For example, T cells may be isolated from a patient by routine techniques (such as by Ficoll/Hypaque density gradient centrifugation of peripheral blood lymphocytes). T cells may be incubated in vitro for 2-9 days (typically 4 days) at 37°C with prostate tumor polypeptide (e.g., 5 - 25 µg/ml). It may be desirable to incubate another aliquot of a T cell sample in the absence of prostate tumor polypeptide to serve as a control. For CD4<sup>+</sup> T cells, activation is preferably detected by evaluating proliferation of the T cells. For CD8+ T cells, activation is preferably detected by evaluating cytolytic activity. A level of proliferation that is at least two fold greater and/or a level of cytolytic activity that is at least 20% greater than in disease-free patients indicates the presence of a cancer in the patient.

As noted above, a cancer may also, or alternatively, be detected based on the level of mRNA encoding a prostate tumor protein in a biological sample. For example, at least two oligonucleotide primers may be employed in a polymerase chain reaction (PCR) based assay to amplify a portion of a prostate tumor cDNA derived from a biological sample, wherein at least one of the oligonucleotide primers is specific for (*i.e.*, hybridizes to) a polynucleotide encoding the prostate tumor protein. The amplified cDNA is then separated and detected using techniques well known in the art, such as gel electrophoresis. Similarly, oligonucleotide probes that specifically hybridize to a polynucleotide encoding a prostate tumor protein may be used in a hybridization assay to detect the presence of polynucleotide encoding the tumor protein in a biological sample.

To permit hybridization under assay conditions, oligonucleotide primers and probes should comprise an oligonucleotide sequence that has at least about 60%, preferably at least about 75% and more preferably at least about 90%, identity to a portion of a polynucleotide encoding a prostate tumor protein that is at least 10 nucleotides, and preferably at least 20 nucleotides, in length. Preferably, oligonucleotide primers and/or probes will hybridize to a polynucleotide encoding a polypeptide disclosed herein under moderately stringent conditions, as defined above. Oligonucleotide primers and/or probes which may be usefully employed in the diagnostic methods described herein preferably are at least 10-40 nucleotides in length. In a preferred embodiment, the oligonucleotide primers

comprise at least 10 contiguous nucleotides, more preferably at least 15 contiguous nucleotides, of a DNA molecule having a sequence recited in SEQ ID NO: 1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375 and 381. Techniques for both PCR based assays and hybridization assays are well known in the art (see, for example, Mullis et al., Cold Spring Harbor Symp. Quant. Biol., 51:263, 1987; Erlich ed., PCR Technology, Stockton Press, NY, 1989).

One preferred assay employs RT-PCR, in which PCR is applied in conjunction with reverse transcription. Typically, RNA is extracted from a biological sample, such as biopsy tissue, and is reverse transcribed to produce cDNA molecules. PCR amplification using at least one specific primer generates a cDNA molecule, which may be separated and visualized using, for example, gel electrophoresis. Amplification may be performed on biological samples taken from a test patient and from an individual who is not afflicted with a cancer. The amplification reaction may be performed on several dilutions of cDNA spanning two orders of magnitude. A two-fold or greater increase in expression in several dilutions of the test patient sample as compared to the same dilutions of the non-cancerous sample is typically considered positive.

In another embodiment, the disclosed compositions may be used as markers for the progression of cancer. In this embodiment, assays as described above for the diagnosis of a cancer may be performed over time, and the change in the level of reactive polypeptide(s) or polynucleotide evaluated. For example, the assays may be performed every 24-72 hours for a period of 6 months to 1 year, and thereafter performed as needed. In general, a cancer is progressing in those patients in whom the level of polypeptide or polynucleotide detected increases over time. In contrast, the cancer is not progressing when the level of reactive polypeptide or polynucleotide either remains constant or decreases with time.

Certain *in vivo* diagnostic assays may be performed directly on a tumor. One such assay involves contacting tumor cells with a binding agent. The bound binding agent may then be detected directly or indirectly via a reporter group. Such binding agents may also be used in histological applications. Alternatively, polynucleotide probes may be used within such applications.

As noted above, to improve sensitivity, multiple prostate tumor protein markers may be assayed within a given sample. It will be apparent that binding agents specific for different proteins provided herein may be combined within a single assay. Further, multiple primers or probes may be used concurrently. The selection of tumor protein markers may be based on routine experiments to determine combinations that results in optimal sensitivity. In addition, or alternatively, assays for tumor proteins provided herein may be combined with assays for other known tumor antigens.

#### DIAGNOSTIC KITS

The present invention further provides kits for use within any of the above diagnostic methods. Such kits typically comprise two or more components necessary for performing a diagnostic assay. Components may be compounds, reagents, containers and/or equipment. For example, one container within a kit may contain a monoclonal antibody or fragment thereof that specifically binds to a prostate tumor protein. Such antibodies or fragments may be provided attached to a support material, as described above. One or more additional containers may enclose elements, such as reagents or buffers, to be used in the assay. Such kits may also, or alternatively, contain a detection reagent as described above that contains a reporter group suitable for direct or indirect detection of antibody binding.

Alternatively, a kit may be designed to detect the level of mRNA encoding a prostate tumor protein in a biological sample. Such kits generally comprise at least one oligonucleotide probe or primer, as described above, that hybridizes to a polynucleotide encoding a prostate tumor protein. Such an oligonucleotide may be used, for example, within a PCR or hybridization assay. Additional components that may be present within such kits include a second oligonucleotide and/or a diagnostic reagent or container to facilitate the detection of a polynucleotide encoding a prostate tumor protein.

The following Examples are offered by way of illustration and not by way of limitation.

#### **EXAMPLES**

#### **EXAMPLE 1**

### ISOLATION AND CHARACTERIZATION OF PROSTATE TUMOR POLYPEPTIDES

This Example describes the isolation of certain prostate tumor polypeptides from a prostate tumor cDNA library.

A human prostate tumor cDNA expression library was constructed from prostate tumor poly A\* RNA using a Superscript Plasmid System for cDNA Synthesis and Plasmid Cloning kit (BRL Life Technologies, Gaithersburg, MD 20897) following the manufacturer's protocol. Specifically, prostate tumor tissues were homogenized with polytron (Kinematica, Switzerland) and total RNA was extracted using Trizol reagent (BRL Life Technologies) as directed by the manufacturer. The poly A\* RNA was then purified using a Qiagen oligotex spin column mRNA purification kit (Qiagen, Santa Clarita, CA 91355) according to the manufacturer's protocol. First-strand cDNA was synthesized using the Notl/Oligo-dT18 primer. Double-stranded cDNA was synthesized, ligated with EcoRI/BAXI adaptors (Invitrogen, San Diego, CA) and digested with Notl. Following size fractionation with Chroma Spin-1000 columns (Clontech, Palo Alto, CA), the cDNA was ligated into the EcoRI/Notl site of pCDNA3.1 (Invitrogen) and transformed into ElectroMax *E. coli* DH10B cells (BRL Life Technologies) by electroporation.

Using the same procedure, a normal human pancreas cDNA expression library was prepared from a pool of six tissue specimens (Clontech). The cDNA libraries were characterized by determining the number of independent colonies, the percentage of clones that carried insert, the average insert size and by sequence analysis. The prostate tumor library contained 1.64 x 10<sup>7</sup> independent colonies, with 70% of clones having an insert and the average insert size being 1745 base pairs. The normal pancreas cDNA library contained 3.3 x 10<sup>6</sup> independent colonies, with 69% of clones having inserts and the average insert size being 1120 base pairs. For both libraries, sequence analysis showed that the majority of clones had a full length cDNA sequence and were synthesized from mRNA, with minimal rRNA and mitochondrial DNA contamination.

cDNA library subtraction was performed using the above prostate tumor and normal pancreas cDNA libraries, as described by Hara et al. (Blood, 84:189-199, 1994) with some modifications. Specifically, a prostate tumor-specific subtracted cDNA library was generated as follows. Normal pancreas cDNA library (70 µg) was digested with EcoRI, NotI, and SfuI, followed by a filling-in reaction with DNA polymerase Klenow fragment. After phenol-chloroform extraction and ethanol precipitation, the DNA was dissolved in 100 µl of

 $H_2O$ , heat-denatured and mixed with 100 µl (100 µg) of Photoprobe biotin (Vector Laboratories, Burlingame, CA). As recommended by the manufacturer, the resulting mixture was irradiated with a 270 W sunlamp on ice for 20 minutes. Additional Photoprobe biotin (50 µl) was added and the biotinylation reaction was repeated. After extraction with butanol five times, the DNA was ethanol-precipitated and dissolved in 23 µl  $H_2O$  to form the driver DNA.

To form the tracer DNA, 10 μg prostate tumor cDNA library was digested with BamHI and XhoI, phenol chloroform extracted and passed through Chroma spin-400 columns (Clontech). Following ethanol precipitation, the tracer DNA was dissolved in 5 μl H<sub>2</sub>O. Tracer DNA was mixed with 15 μl driver DNA and 20 μl of 2 x hybridization buffer (1.5 M NaCl/10 mM EDTA/50 mM HEPES pH 7.5/0.2% sodium dodecyl sulfate), overlaid with mineral oil, and heat-denatured completely. The sample was immediately transferred into a 68 °C water bath and incubated for 20 hours (long hybridization [LH]). The reaction mixture was then subjected to a streptavidin treatment followed by phenol/chloroform extraction. This process was repeated three more times. Subtracted DNA was precipitated, dissolved in 12 μl H<sub>2</sub>O, mixed with 8 μl driver DNA and 20 μl of 2 x hybridization buffer, and subjected to a hybridization at 68 °C for 2 hours (short hybridization [SH]). After removal of biotinylated double-stranded DNA, subtracted cDNA was ligated into BamHI/XhoI site of chloramphenicol resistant pBCSK+ (Stratagene, La Jolla, CA 92037) and transformed into ElectroMax *E. coli* DH10B cells by electroporation to generate a prostate tumor specific subtracted cDNA library (referred to as "prostate subtraction 1").

To analyze the subtracted cDNA library, plasmid DNA was prepared from 100 independent clones, randomly picked from the subtracted prostate tumor specific library and grouped based on insert size. Representative cDNA clones were further characterized by DNA sequencing with a Perkin Elmer/Applied Biosystems Division Automated Sequencer Model 373A (Foster City, CA). Six cDNA clones, hereinafter referred to as F1-13, F1-12, F1-16, H1-1, H1-9 and H1-4, were shown to be abundant in the subtracted prostate-specific cDNA library. The determined 3' and 5' cDNA sequences for F1-12 are provided in SEQ ID NO: 2 and 3, respectively, with determined 3' cDNA sequences for F1-13, F1-16, H1-1, H1-9 and H1-4 being provided in SEQ ID NO: 1 and 4-7, respectively.

The cDNA sequences for the isolated clones were compared to known sequences in the gene bank using the EMBL and GenBank databases (release 96). Four of the prostate tumor cDNA clones, F1-13, F1-16, H1-1, and H1-4, were determined to encode the following previously identified proteins: prostate specific antigen (PSA), human glandular kallikrein, human tumor expression enhanced gene, and mitochondria cytochrome C oxidase subunit II. H1-9 was found to be identical to a previously identified human

autonomously replicating sequence. No significant homologies to the cDNA sequence for F1-12 were found.

Subsequent studies led to the isolation of a full-length cDNA sequence for F1-12. This sequence is provided in SEQ ID NO: 107, with the corresponding predicted amino acid sequence being provided in SEQ ID NO: 108.

To clone less abundant prostate tumor specific genes, cDNA library subtraction was performed by subtracting the prostate tumor cDNA library described above with the normal pancreas cDNA library and with the three most abundant genes in the previously subtracted prostate tumor specific cDNA library: human glandular kallikrein, prostate specific antigen (PSA), and mitochondria cytochrome C oxidase subunit II. Specifically, 1 µg each of human glandular kallikrein, PSA and mitochondria cytochrome C oxidase subunit II cDNAs in pCDNA3.1 were added to the driver DNA and subtraction was performed as described above to provide a second subtracted cDNA library hereinafter referred to as the "subtracted prostate tumor specific cDNA library with spike".

Twenty-two cDNA clones were isolated from the subtracted prostate tumor specific cDNA library with spike. The determined 3' and 5' cDNA sequences for the clones referred to as J1-17, L1-12, N1-1862, J1-13, J1-19, J1-25. J1-24, K1-58, K1-63, L1-4 and L1-14 are provided in SEQ ID NOS: 8-9, 10-11, 12-13, 14-15, 16-17, 18-19, 20-21, 22-23, 24-25, 26-27 and 28-29, respectively. The determined 3' cDNA sequences for the clones referred to as J1-12, J1-16, J1-21, K1-48, K1-55, L1-2, L1-6, N1-1858, N1-1860, N1-1861, N1-1864 are provided in SEQ ID NOS: 30-40, respectively. Comparison of these sequences with those in the gene bank as described above, revealed no significant homologies to three of the five most abundant DNA species, (J1-17, L1-12 and N1-1862; SEQ ID NOS: 8-9, 10-11 and 12-13, respectively). Of the remaining two most abundant species, one (J1-12; SEQ ID NO:30) was found to be identical to the previously identified human pulmonary surfactant-associated protein, and the other (K1-48; SEQ ID NO:33) was determined to have some homology to R. norvegicus mRNA for 2-arylpropionyl-CoA epimerase. Of the 17 less abundant cDNA clones isolated from the subtracted prostate tumor specific cDNA library with spike, four (J1-16. K1-55, L1-6 and N1-1864; SEQ ID NOS:31, 34, 36 and 40, respectively) were found to be identical to previously identified sequences, two (J1-21 and N1-1860; SEQ ID NOS: 32 and 38, respectively) were found to show some homology to non-human sequences, and two (L1-2 and N1-1861; SEQ ID NOS: 35 and 39, respectively) were found to show some homology to known human sequences. No significant homologies were found to the polypeptides J1-13, J1-19, J1-24, J1-25, K1-58, K1-63, L1-4, L1-14 (SEQ ID NOS: 14-15, 16-17, 20-21, 18-19, 22-23, 24-25, 26-27, 28-29, respectively).

Subsequent studies led to the isolation of full length cDNA sequences for J1-17, L1-12 and N1-1862 (SEQ ID NOS: 109-111, respectively). The corresponding predicted

amino acid sequences are provided in SEQ ID NOS: 112-114. L1-12 is also referred to as P501S.

In a further experiment, four additional clones were identified by subtracting a prostate tumor cDNA library with normal prostate cDNA prepared from a pool of three normal prostate poly A+ RNA (referred to as "prostate subtraction 2"). The determined cDNA sequences for these clones, hereinafter referred to as U1-3064, U1-3065, V1-3692 and 1A-3905, are provided in SEQ ID NO: 69-72, respectively. Comparison of the determined sequences with those in the gene bank revealed no significant homologies to U1-3065.

A second subtraction with spike (referred to as "prostate subtraction spike 2") was performed by subtracting a prostate tumor specific cDNA library with spike with normal pancreas cDNA library and further spiked with PSA, J1-17, pulmonary surfactant-associated protein, mitochondrial DNA, cytochrome c oxidase subunit II, N1-1862, autonomously replicating sequence, L1-12 and tumor expression enhanced gene. Four additional clones, hereinafter referred to as V1-3686, R1-2330, 1B-3976 and V1-3679, were isolated. The determined cDNA sequences for these clones are provided in SEQ ID NO:73-76, respectively. Comparison of these sequences with those in the gene bank revealed no significant homologies to V1-3686 and R1-2330.

Further analysis of the three prostate subtractions described above (prostate subtraction 2, subtracted prostate tumor specific cDNA library with spike, and prostate subtraction spike 2) resulted in the identification of sixteen additional clones, referred to as 1G-4736, 1G-4738, 1G-4741, 1G-4744, 1G-4734, 1H-4774, 1H-4781, 1H-4785, 1H-4787, 1H-4796, 1I-4810, 1I-4811, 1J-4876, 1K-4884 and 1K-4896. The determined cDNA sequences for these clones are provided in SEQ ID NOS: 77-92, respectively. Comparison of these sequences with those in the gene bank as described above, revealed no significant homologies to 1G-4741, 1G-4734, 1I-4807, 1J-4876 and 1K-4896 (SEQ ID NOS: 79, 81, 87, 90 and 92, respectively). Further analysis of the isolated clones led to the determination of extended cDNA sequences for 1G-4736, 1G-4738, 1G-4741, 1G-4744, 1H-4774, 1H-4781, 1H-4785, 1H-4787, 1H-4796, 1I-4807, 1J-4876, 1K-4884 and 1K-4896, provided in SEQ ID NOS: 179-188 and 191-193, respectively, and to the determination of additional partial cDNA sequences for 1I-4810 and 1I-4811, provided in SEQ ID NOS: 189 and 190, respectively.

Additional studies with prostate subtraction spike 2 resulted in the isolation of three more clones. Their sequences were determined as described above and compared to the most recent GenBank. All three clones were found to have homology to known genes, which are Cysteine-rich protein, KIAA0242, and KIAA0280 (SEQ ID NO: 317, 319, and 320, respectively). Further analysis of these clones by Synteni microarray (Synteni, Palo Alto, CA) demonstrated that all three clones were over-expressed in most prostate tumors and

prostate BPH, as well as in the majority of normal prostate tissues tested, but low expression in all other normal tissues.

An additional subtraction was performed by subtracting a normal prostate cDNA library with normal pancreas cDNA (referred to as "prostate subtraction 3"). This led to the identification of six additional clones referred to as 1G-4761, 1G-4762, 1H-4766, 1H-4770, 1H-4771 and 1H-4772 (SEQ ID NOS: 93-98). Comparison of these sequences with those in the gene bank revealed no significant homologies to 1G-4761 and 1H-4771 (SEQ ID NOS: 93 and 97, respectively). Further analysis of the isolated clones led to the determination of extended cDNA sequences for 1G-4761, 1G-4762, 1H-4766 and 1H-4772 provided in SEQ ID NOS: 194-196 and 199, respectively, and to the determination of additional partial cDNA sequences for 1H-4770 and 1H-4771, provided in SEQ ID NOS: 197 and 198, respectively.

Subtraction of a prostate tumor cDNA library, prepared from a pool of polyA+RNA from three prostate cancer patients, with a normal pancreas cDNA library (prostate subtraction 4) led to the identification of eight clones, referred to as 1D-4297, 1D-4309, 1D.1-4278, 1D-4283, 1D-4304, 1D-4296 and 1D-4280 (SEQ ID NOS: 99-107). These sequences were compared to those in the gene bank as described above. No significant homologies were found to 1D-4283 and 1D-4304 (SEQ ID NOS: 103 and 104, respectively). Further analysis of the isolated clones led to the determination of extended cDNA sequences for 1D-4309, 1D.1-4278, 1D-4288, 1D-4283, 1D-4304, 1D-4296 and 1D-4280, provided in SEQ ID NOS: 200-206, respectively.

cDNA clones isolated in prostate subtraction 1 and prostate subtraction 2, described above, were colony PCR amplified and their mRNA expression levels in prostate tumor, normal prostate and in various other normal tissues were determined using microarray technology (Synteni, Palo Alto, CA). Briefly, the PCR amplification products were dotted onto slides in an array format, with each product occupying a unique location in the array. mRNA was extracted from the tissue sample to be tested, reverse transcribed, and fluorescent-labeled cDNA probes were generated. The microarrays were probed with the labeled cDNA probes, the slides scanned and fluorescence intensity was measured. This intensity correlates with the hybridization intensity. Two clones (referred to as P509S and P510S) were found to be over-expressed in prostate tumor and normal prostate and expressed at low levels in all other normal tissues tested (liver, pancreas, skin, bone marrow, brain, breast, adrenal gland, bladder, testes, salivary gland, large intestine, kidney, ovary, lung, spinal cord, skeletal muscle and colon). The determined cDNA sequences for P509S and P510S are provided in SEQ ID NO: 223 and 224, respectively. Comparison of these sequences with those in the gene bank as described above, revealed some homology to previously identified ESTs.

Additional, studies led to the isolation of the full-length cDNA sequence for P509S. This sequence is provided in SEQ ID NO: 332, with the corresponding predicted amino acid sequence being provided in SEQ ID NO: 339.

### EXAMPLE 2

### DETERMINATION OF TISSUE SPECIFICITY OF PROSTATE TUMOR POLYPEPTIDES

Using gene specific primers, mRNA expression levels for the representative prostate tumor polypeptides F1-16, H1-1, J1-17 (also referred to as P502S), L1-12 (also referred to as P501S), F1-12 (also referred to as P504S) and N1-1862 (also referred to as P503S) were examined in a variety of normal and tumor tissues using RT-PCR.

Briefly, total RNA was extracted from a variety of normal and tumor tissues using Trizol reagent as described above. First strand synthesis was carried out using 1-2  $\mu$ g of total RNA with SuperScript II reverse transcriptase (BRL Life Technologies) at 42 °C for one hour. The cDNA was then amplified by PCR with gene-specific primers. To ensure the semi-quantitative nature of the RT-PCR,  $\beta$ -actin was used as an internal control for each of the tissues examined. First, serial dilutions of the first strand cDNAs were prepared and RT-PCR assays were performed using  $\beta$ -actin specific primers. A dilution was then chosen that enabled the linear range amplification of the  $\beta$ -actin template and which was sensitive enough to reflect the differences in the initial copy numbers. Using these conditions, the  $\beta$ -actin levels were determined for each reverse transcription reaction from each tissue. DNA contamination was minimized by DNase treatment and by assuring a negative PCR result when using first strand cDNA that was prepared without adding reverse transcriptase.

mRNA Expression levels were examined in four different types of tumor tissue (prostate tumor from 2 patients, breast tumor from 3 patients, colon tumor, lung tumor), and sixteen different normal tissues, including prostate, colon, kidney, liver, lung, ovary, pancreas, skeletal muscle, skin, stomach, testes, bone marrow and brain. F1-16 was found to be expressed at high levels in prostate tumor tissue, colon tumor and normal prostate, and at lower levels in normal liver, skin and testes, with expression being undetectable in the other tissues examined. H1-1 was found to be expressed at high levels in prostate tumor, lung tumor, breast tumor, normal prostate, normal colon and normal brain, at much lower levels in normal lung, pancreas, skeletal muscle, skin, small intestine, bone marrow, and was not detected in the other tissues tested. J1-17 (P502S) and L1-12 (P501S) appear to be specifically over-expressed in prostate, with both genes being expressed at high levels in prostate tumor and normal prostate but at low to undetectable levels in all the other tissues examined. N1-1862 (P503S) was found to be over-expressed in 60% of prostate tumors and detectable in normal colon and kidney. The RT-PCR results thus indicate that

F1-16, H1-1, J1-17 (P502S), N1-1862 (P503S) and L1-12 (P501S) are either prostate specific or are expressed at significantly elevated levels in prostate.

Further RT-PCR studies showed that F1-12 (P504S) is over-expressed in 60% of prostate tumors, detectable in normal kidney but not detectable in all other tissues tested. Similarly, R1-2330 was shown to be over-expressed in 40% of prostate tumors, detectable in normal kidney and liver, but not detectable in all other tissues tested. U1-3064 was found to be over-expressed in 60% of prostate tumors, and also expressed in breast and colon tumors, but was not detectable in normal tissues.

RT-PCR characterization of R1-2330, U1-3064 and 1D-4279 showed that these three antigens are over-expressed in prostate and/or prostate tumors.

Northern analysis with four prostate tumors, two normal prostate samples, two BPH prostates, and normal colon, kidney, liver, lung, pancrease, skeletal muscle, brain, stomach, testes, small intestine and bone marrow, showed that L1-12 (P501S) is over-expressed in prostate tumors and normal prostate, while being undetectable in other normal tissues tested. J1-17 (P502S) was detected in two prostate tumors and not in the other tissues tested. N1-1862 (P503S) was found to be over-expressed in three prostate tumors and to be expressed in normal prostate, colon and kidney, but not in other tissues tested. F1-12 (P504S) was found to be highly expressed in two prostate tumors and to be undetectable in all other tissues tested.

The microarray technology described above was used to determine the expression levels of representative antigens described herein in prostate tumor, breast tumor and the following normal tissues: prostate, liver, pancreas, skin, bone marrow, brain, breast, adrenal gland, bladder, testes, salivary gland, large intestine, kidney, ovary, lung, spinal cord, skeletal muscle and colon. L1-12 (P501S) was found to be over-expressed in normal prostate and prostate tumor, with some expression being detected in normal skeletal muscle. Both J1-12 and F1-12 (P504S) were found to be over-expressed in prostate tumor, with expression being lower or undetectable in all other tissues tested. N1-1862 (P503S) was found to be expressed at high levels in prostate tumor and normal prostate, and at low levels in normal large intestine and normal colon, with expression being undetectable in all other tissues tested. R1-2330 was found to be over-expressed in prostate tumor and normal prostate, and to be expressed at lower levels in all other tissues tested. 1D-4279 was found to be over-expressed in prostate tumor and normal spinal cord, and to be undetectable in all other tissues tested.

Further microarray analysis to specifically address the extent to which P501S (SEQ ID NO: 110) was expressed in breast tumor revealed moderate over-expression not only in breast tumor, but also in metastatic breast tumor (2/31), with negligible to low expression

in normal tissues. This data suggests that P501S may be over-expressed in various breast tumors as well as in prostate tumors.

The expression levels of 32 ESTs (expressed sequence tags) described by Vasmatzis et al. (Proc. Natl. Acad. Sci. USA 95:300-304, 1998) in a variety of tumor and normal tissues were examined by microarray technology as described above. Two of these clones (referred to as P1000C and P1001C) were found to be over-expressed in prostate tumor and normal prostate, and expressed at low to undetectable levels in all other tissues tested (normal aorta, thymus, resting and activated PBMC, epithelial cells, spinal cord, adrenal gland, fetal tissues, skin, salivary gland, large intestine, bone marrow, liver, lung, dendritic cells, stomach, lymph nodes, brain, heart, small intestine, skeletal muscle, colon and kidney. The determined cDNA sequences for P1000C and P1001C are provided in SEQ ID NO: 384 and 472, respectively. The sequence of P1001C was found to show some homology to the previously isolated Human mRNA for JM27 protein. No significant homologies were found to the sequence of P1000C.

The expression of the polypeptide encoded by the full length cDNA sequence for F1-12 (also referred to as P504S; SEQ ID NO: 108) was investigated by immunohistochemical analysis. Rabbit-anti-P504S polyclonal antibodies were generated against the full length P504S protein by standard techniques. Subsequent isolation and characterization of the polyclonal antibodies were also performed by techniques well known in the art. Immunohistochemical analysis showed that the P504S polypeptide was expressed in 100% of prostate carcinoma samples tested (n=5).

The rabbit-anti-P504S polyclonal antibody did not appear to label benign prostate cells with the same cytoplasmic granular staining, but rather with light nuclear staining. Analysis of normal tissues revealed that the encoded polypeptide was found to be expressed in some, but not all normal human tissues. Positive cytoplasmic staining with rabbit-anti-P504S polyclonal antibody was found in normal human kidney, liver, brain, colon and lung-associated macrophages, whereas heart and bone marrow were negative.

This data indicates that the P504S polypeptide is present in prostate cancer tissues, and that there are qualitative and quantitative differences in the staining between benign prostatic hyperplasia tissues and prostate cancer tissues, suggesting that this polypeptide may be detected selectively in prostate tumors and therefore be useful in the diagnosis of prostate cancer.

### **EXAMPLE 3**

ISOLATION AND CHARACTERIZATION OF PROSTATE TUMOR POLYPEPTIDES BY PCR-BASED SUBTRACTION

A cDNA subtraction library, containing cDNA from normal prostate\_subtracted with ten other normal tissue cDNAs (brain, heart, kidney, liver, lung, ovary, placenta, skeletal muscle, spleen and thymus) and then submitted to a first round of PCR amplification, was purchased from Clontech. This library was subjected to a second round of PCR amplification, following the manufacturer's protocol. The resulting cDNA fragments were subcloned into the vector pT7 Blue T-vector (Novagen, Madison, WI) and transformed into XL-1 Blue MRF' E. coli (Stratagene). DNA was isolated from independent clones and sequenced using a Perkin Elmer/Applied Biosystems Division Automated Sequencer Model 373A.

Fifty-nine positive clones were sequenced. Comparison of the DNA sequences of these clones with those in the gene bank, as described above, revealed no significant homologies to 25 of these clones, hereinafter referred to as P5, P8, P9, P18, P20, P30, P34, P36, P38, P39, P42, P49, P50, P53, P55, P60, P64, P65, P73, P75, P76, P79 and P84. The determined cDNA sequences for these clones are provided in SEQ ID NO: 41-45, 47-52 and 54-65, respectively. P29, P47, P68, P80 and P82 (SEQ ID NO: 46, 53 and 66-68, respectively) were found to show some degree of homology to previously identified DNA sequences. To the best of the inventors' knowledge, none of these sequences have been previously shown to be present in prostate.

Further studies using the PCR-based methodology described above resulted in the isolation of more than 180 additional clones, of which 23 clones were found to show no significant homologies to known sequences. The determined cDNA sequences for these clones are provided in SEQ ID NO: 115-123, 127, 131, 137, 145, 147-151, 153, 156-158 and 160. Twenty-three clones (SEQ ID NO: 124-126, 128-130, 132-136, 138-144, 146, 152, 154, 155 and 159) were found to show some homology to previously identified ESTs. An additional ten clones (SEQ ID NO: 161-170) were found to have some degree of homology to known genes. Larger cDNA clones containing the P20 sequence represent splice variants of a gene referred to as P703P. The determined DNA sequence for the variants referred to as DE1, DE13 and DE14 are provided in SEQ ID NOS: 171, 175 and 177, respectively, with the corresponding predicted amino acid sequences being provided in SEQ ID NO: 172, 176 and 178, respectively. The determined cDNA sequence for an extended spliced form of P703 is provided in SEQ ID NO: 225. The DNA sequences for the splice variants referred to as DE2 and DE6 are provided in SEQ ID NOS: 173 and 174, respectively.

mRNA Expression levels for representative clones in tumor tissues (prostate (n=5), breast (n=2), colon and lung) normal tissues (prostate (n=5), colon, kidney, liver, lung (n=2), ovary (n=2), skeletal muscle, skin, stomach, small intestine and brain), and activated

and non-activated PBMC was determined by RT-PCR as described above. Expression was examined in one sample of each tissue type unless otherwise indicated.

P9 was found to be highly expressed in normal prostate and prostate tumor compared to all normal tissues tested except for normal colon which showed comparable expression. P20, a portion of the P703P gene, was found to be highly expressed in normal prostate and prostate tumor, compared to all twelve normal tissues tested. A-modest increase in expression of P20 in breast tumor (n=2), colon tumor and lung tumor was seen compared to all normal tissues except lung (1 of 2). Increased expression of P18 was found in normal prostate, prostate tumor and breast tumor compared to other normal tissues except lung and stomach. A modest increase in expression of P5 was observed in normal prostate compared to most other normal tissues. However, some elevated expression was seen in normal lung and PBMC. Elevated expression of P5 was also observed in prostate tumors (2 of 5), breast tumor and one lung tumor sample. For P30, similar expression levels were seen in normal prostate and prostate tumor, compared to six of twelve other normal tissues tested. Increased expression was seen in breast tumors, one lung tumor sample and one colon tumor sample, and also in normal PBMC. P29 was found to be over-expressed in prostate tumor (5 of 5) and normal prostate (5 of 5) compared to the majority of normal tissues. However, substantial expression of P29 was observed in normal colon and normal lung (2 of 2). P80 was found to be over-expressed in prostate tumor (5 of 5) and normal prostate (5 of 5) compared to all other normal tissues tested, with increased expression also being seen in colon tumor.

Further studies resulted in the isolation of twelve additional clones, hereinafter referred to as 10-d8, 10-h10, 11-c8, 7-g6, 8-b5, 8-b6, 8-d4, 8-d9, 8-g3, 8-h11, 9-f12 and 9-f3. The determined DNA sequences for 10-d8, 10-h10, 11-c8, 8-d4, 8-d9, 8-h11, 9-f12 and 9-f3 are provided in SEQ ID NO: 207, 208, 209, 216, 217, 220, 221 and 222, respectively. The determined forward and reverse DNA sequences for 7-g6, 8-b5, 8-b6 and 8-g3 are provided in SEQ ID NO: 210 and 211; 212 and 213; 214 and 215; and 218 and 219, respectively. Comparison of these sequences with those in the gene bank revealed no significant homologies to the sequence of 9-f3. The clones 10-d8, 11-c8 and 8-h11 were found to show some homology to previously isolated ESTs, while 10-h10, 8-b5, 8-b6, 8-d4, 8-d9, 8-g3 and 9-f12 were found to show some homology to previously identified genes. Further characterization of 7-G6 and 8-G3 showed identity to the known genes PAP and PSA, respectively.

mRNA expression levels for these clones were determined using the micro-array technology described above. The clones 7-G6, 8-G3, 8-B5, 8-B6, 8-D4, 8-D9, 9-F3, 9-F12, 9-H3, 10-A2, 10-A4, 11-C9 and 11-F2 were found to be over-expressed in prostate tumor and normal prostate, with expression in other tissues tested being low or undetectable.

Increased expression of 8-F11 was seen in prostate tumor and normal prostate, bladder, skeletal muscle and colon. Increased expression of 10-H10 was seen in prostate tumor and normal prostate, bladder, lung, colon, brain and large intestine. Increased expression of 9-B1 was seen in prostate tumor, breast tumor, and normal prostate, salivary gland, large intestine and skin, with increased expression of 11-C8 being seen in prostate tumor, and normal prostate and large intestine.

An additional cDNA fragment derived from the PCR-based normal prostate subtraction, described above, was found to be prostate specific by both micro-array technology and RT-PCR. The determined cDNA sequence of this clone (referred to as 9-A11) is provided in SEQ ID NO: 226. Comparison of this sequence with those in the public databases revealed 99% identity to the known gene HOXB13.

Further studies led to the isolation of the clones 8-C6 and 8-H7. The determined cDNA sequences for these clones are provided in SEQ ID NO: 227 and 228, respectively. These sequences were found to show some homology to previously isolated ESTs.

PCR and hybridization-based methodologies were employed to obtain longer cDNA sequences for clone P20 (also referred to as P703P), yielding three additional cDNA fragments that progressively extend the 5' end of the gene. These fragments, referred to as P703PDE5, P703P6.26, and P703PX-23 (SEQ ID NO: 326, 328 and 330, with the predicted corresponding amino acid sequences being provided in SEQ ID NO: 327, 329 and 331, respectively) contain additional 5' sequence. P703PDE5 was recovered by screening of a cDNA library (#141-26) with a portion of P703P as a probe. P703P6.26 was recovered from a mixture of three prostate tumor cDNAs and P703PX\_23 was recovered from cDNA library (#438-48). Together, the additional sequences include all of the putative mature serine protease along with part of the putative signal sequence. Further studies using a PCR-based subtraction library of a prostate tumor pool subtracted against a pool of normal tissues (referred to as JP: PCR subtraction) resulted in the isolation of thirteen additional clones, seven of which did not share any significant homology to known GenBank sequences. The determined cDNA sequences for these seven clones (P711P, P712P, novel 23, P774P, P775P, P710P and P768P) are provided in SEQ ID NO: 307-311, 313 and 315, respectively. The remaining six clones (SEQ ID NO: 316 and 321-325) were shown to share some homology to known genes. By microarray analysis, all thirteen clones showed three or more fold overexpression in prostate tissues, including prostate tumors, BPH and normal prostate as compared to normal non-prostate tissues. Clones P711P, P712P, novel 23 and P768P showed over-expression in most prostate tumors and BPH tissues tested (n=29), and in the majority of normal prostate tissues (n=4), but background to low expression levels in all normal tissues.

Clones P774P, P775P and P710P showed comparatively lower expression and expression in fewer prostate tumors and BPH samples, with negative to low expression in normal prostate.

The full-length cDNA for P711P was obtained by employing the partial sequence of SEQ ID NO: 307 to screen a prostate cDNA library. Specifically, a directionally cloned prostate cDNA library was prepared using standard techniques. One million colonies of this library were plated onto LB/Amp plates. Nylon membrane filters were used to lift these colonies, and the cDNAs which were picked up by these filters were denatured and cross-linked to the filters by UV light. The P711P cDNA fragment of SEQ ID NO: 307 was radio-labeled and used to hybridize with these filters. Positive clones were selected, and cDNAs were prepared and sequenced using an automatic Perkin Elmer/Applied Biosystems sequencer. The determined full-length sequence of P711P is provided in SEQ ID NO: 382, with the corresponding predicted amino acid sequence being provided in SEQ ID NO: 383.

Using PCR and hybridization-based methodologies, additional cDNA sequence information was derived for two clones described above, 11-C9 and 9-F3, herein after referred to as P707P and P714P, respectively (SEQ ID NO: 333 and 334). After comparison with the most recent GenBank, P707P was found to be a splice variant of the known gene HoxB13. In contrast, no significant homologies to P714P were found.

Clones 8-B3, P89, P98, P130 and P201 (as disclosed in U.S. Patent Application No. 09/020,956, filed February 9, 1998) were found to be contained within one contiguous sequence, referred to as P705P (SEQ ID NO: 335, with the predicted amino acid sequence provided in SEQ ID NO: 336), which was determined to be a splice variant of the known gene NKX 3.1.

### EXAMPLE 4 SYNTHESIS OF POLYPEPTIDES

Polypeptides may be synthesized on a Perkin Elmer/Applied Biosystems 430A peptide synthesizer using FMOC chemistry with HPTU (O-Benzotriazole-N,N,N',N'-tetramethyluronium hexafluorophosphate) activation. A Gly-Cys-Gly sequence may be attached to the amino terminus of the peptide to provide a method of conjugation, binding to an immobilized surface, or labeling of the peptide. Cleavage of the peptides from the solid support may be carried out using the following cleavage mixture: trifluoroacetic acid:ethanedithiol:thioanisole:water:phenol (40:1:2:2:3). After cleaving for 2 hours, the peptides may be precipitated in cold methyl-t-butyl-ether. The peptide pellets may then be dissolved in water containing 0.1% trifluoroacetic acid (TFA) and lyophilized prior to purification by C18 reverse phase HPLC. A gradient of 0%-60% acetonitrile (containing 0.1% TFA) in water (containing 0.1% TFA) may be used to elute the peptides. Following

lyophilization of the pure fractions, the peptides may be characterized using electrospray or other types of mass spectrometry and by amino acid analysis.

#### **EXAMPLE 5**

### FURTHER ISOLATION AND CHARACTERIZATION OF PROSTATE TUMOR POLYPEPTIDES BY PCR-BASED SUBTRACTION

A cDNA library generated from prostate primary tumor mRNA as described above was subtracted with cDNA from normal prostate. The subtraction was performed using a PCR-based protocol (Clontech), which was modified to generate larger fragments. Within this protocol, tester and driver double stranded cDNA were separately digested with five restriction enzymes that recognize six-nucleotide restriction sites (MluI, MscI, PvuII, SalI and StuI). This digestion resulted in an average cDNA size of 600 bp, rather than the average size of 300 bp that results from digestion with RsaI according to the Clontech protocol. This modification did not affect the subtraction efficiency. Two tester populations were then created with different adapters, and the driver library remained without adapters.

The tester and driver libraries were then hybridized using excess driver cDNA. In the first hybridization step, driver was separately hybridized with each of the two tester cDNA populations. This resulted in populations of (a) unhybridized tester cDNAs, (b) tester cDNAs hybridized to other tester cDNAs, (c) tester cDNAs hybridized to driver cDNAs and (d) unhybridized driver cDNAs. The two separate hybridization reactions were then combined, and rehybridized in the presence of additional denatured driver cDNA. Following this second hybridization, in addition to populations (a) through (d), a fifth population (e) was generated in which tester cDNA with one adapter hybridized to tester cDNA with the second adapter. Accordingly, the second hybridization step resulted in enrichment of differentially expressed sequences which could be used as templates for PCR amplification with adaptor-specific primers.

The ends were then filled in, and PCR amplification was performed using adaptor-specific primers. Only population (e), which contained tester cDNA that did not hybridize to driver cDNA, was amplified exponentially. A second PCR amplification step was then performed, to reduce background and further enrich differentially expressed sequences.

This PCR-based subtraction technique normalizes differentially expressed cDNAs so that rare transcripts that are overexpressed in prostate tumor tissue may be recoverable. Such transcripts would be difficult to recover by traditional subtraction methods.

In addition to genes known to be overexpressed in prostate tumor, seventy-seven further clones were identified. Sequences of these partial cDNAs are provided in SEQ\_ID NO: 29 to 305. Most of these clones had no significant homology to database sequences. Exceptions were JPTPN23 (SEQ ID NO: 231; similarity to pig valosin-containing protein), JPTPN30 (SEQ ID NO: 234; similarity to rat mRNA for proteasome subunit), JPTPN45 (SEQ ID NO: 243; similarity to rat norvegicus cytosolic NADP-dependent isocitrate dehydrogenase), JPTPN46 (SEQ ID NO: 244; similarity to human subclone H8 4 d4 DNA sequence), JP1D6 (SEQ ID NO: 265; similarity to G. gallus dynein light chain-A), JP8D6 (SEQ ID NO: 288; similarity to human BAC clone RG016J04), JP8F5 (SEQ ID NO: 289; similarity to human subclone H8 3 b5 DNA sequence), and JP8E9 (SEQ ID NO: 299; similarity to human Alu sequence).

Additional studies using the PCR-based subtraction library consisting of a prostate tumor pool subtracted against a normal prostate pool (referred to as PT-PN PCR subtraction) yielded three additional clones. Comparison of the cDNA sequences of these clones with the most recent release of GenBank revealed no significant homologies to the two clones referred to as P715P and P767P (SEQ ID NO: 312 and 314). The remaining clone was found to show some homology to the known gene KIAA0056 (SEQ ID NO: 318). Using microarray analysis to measure mRNA expression levels in various tissues, all three clones were found to be over-expressed in prostate tumors and BPH tissues. Specifically, clone P715P was over-expressed in most prostate tumors and BPH tissues by a factor of three or greater, with elevated expression seen in the majority of normal prostate samples and in fetal tissue, but negative to low expression in all other normal tissues. Clone P767P was over-expressed in several prostate tumors and BPH tissues, with moderate expression levels in half of the normal prostate samples, and background to low expression in all other normal tissues tested.

Further analysis, by microarray as described above, of the PT-PN PCR subtraction library and of a DNA subtraction library containing cDNA from prostate tumor – subtracted with a pool of normal tissue cDNAs, led to the isolation of 27 additional clones (SEQ ID NO: 340-365 and 381) which were determined to be over-expressed in prostate tumor. The clones of SEQ ID NO: 341, 342, 345, 347, 348, 349, 351, 355-359, 361, 362 and 364 were also found to be expressed in normal prostate. Expression of all 26 clones in a variety of normal tissues was found to be low or undetectable, with the exception of P544S (SEQ ID NO: 356) which was found to be expressed in small intestine. Of the 26 clones, 10 (SEQ ID NO: 340-349) were found to show some homology to previously identified sequences. No significant homologies were found to the clones of SEQ ID NO: 350-365.

### EXAMPLE 6 PEPTIDE PRIMING OF MICE AND PROPAGATION OF CTL LINES

6.1. This Example illustrates the preparation of a CTL cell line specific for cells expressing the P502S gene.

Mice expressing the transgene for human HLA A2.1 (provided by Dr L. Sherman, The Scripps Research Institute, La Jolla, CA) were immunized with P2S#12 peptide (VLGWVAEL; SEQ ID NO: 306), which is derived from the P502S gene (also referred to herein as J1-17, SEQ ID NO: 8), as described by Theobald et al., Proc. Natl. Acad. Sci. USA 92:11993-11997, 1995 with the following modifications. Mice were immunized with 100µg of P2S#12 and 120µg of an I-Ab binding peptide derived from hepatitis B Virus protein emulsified in incomplete Freund's adjuvant. Three weeks later these mice were sacrificed and using a nylon mesh single cell suspensions prepared. Cells were then resuspended at 6 x 106 cells/ml in complete media (RPMI-1640; Gibco BRL, Gaithersburg, MD) containing 10% FCS, 2mM Glutamine (Gibco BRL), sodium pyruvate (Gibco BRL), non-essential amino acids (Gibco BRL), 2 x 10<sup>-5</sup> M 2-mercaptoethanol, 50U/ml penicillin and streptomycin, and cultured in the presence of irradiated (3000 rads) P2S#12-pulsed (5mg/ml P2S#12 and 10mg/ml β2-microglobulin) LPS blasts (A2 transgenic spleens cells cultured in the presence of  $7\mu g/ml$  dextran sulfate and  $25\mu g/ml$  LPS for 3 days). Six days later, cells (5 x 105/ml) were restimulated with 2.5 x 106/ml peptide pulsed irradiated (20,000 rads) EL4A2Kb cells (Sherman et al, Science 258:815-818, 1992) and 3 x 106/ml A2 transgenic spleen feeder cells. Cells were cultured in the presence of 20U/ml IL-2. Cells continued to be restimulated on a weekly basis as described, in preparation for cloning the line.

P2S#12 line was cloned by limiting dilution analysis with peptide pulsed EL4 A2Kb tumor cells (1 x  $10^4$  cells/ well) as stimulators and A2 transgenic spleen cells as feeders (5 x  $10^5$  cells/ well) grown in the presence of 30U/ml IL-2. On day 14, cells were

restimulated as before. On day 21, clones that were growing were isolated and maintained in culture. Several of these clones demonstrated significantly higher reactivity (lysis) against \_human fibroblasts (HLA A2.1 expressing) transduced with P502S than against control fibroblasts. An example is presented in Figure 1.

This data indicates that P2S #12 represents a naturally processed epitope of the P502S protein that is expressed in the context of the human HLA A2.1 molecule.

6.2. This Example illustrates the preparation of murine CTL lines and CTL clones specific for cells expressing the P501S gene.

This series of experiments were performed similarly to that described above. Mice were immunized with the P1S#10 peptide (SEQ ID NO: 337), which is derived from the P501S gene (also referred to herein as L1-12, SEQ ID NO: 110). The P1S#10 peptide was derived by analysis of the predicted polypeptide sequence for P501S for potential HLA-A2 binding sequences as defined by published HLA-A2 binding motifs (Parker, KC, et al, J. Immunol., 152:163, 1994). P1S#10 peptide was synthesized as described in Example 4, and empirically tested for HLA-A2 binding using a T cell based competition assay. Predicted A2 binding peptides were tested for their ability to compete HLA-A2 specific peptide presentation to an HLA-A2 restricted CTL clone (D150M58), which is specific for the HLA-A2 binding influenza matrix peptide fluM58. D150M58 CTL secretes TNF in response to self-presentation of peptide fluM58. In the competition assay, test peptides at 100-200 µg/ml were added to cultures of D150M58 CTL in order to bind HLA-A2 on the CTL. After thirty minutes, CTL cultured with test peptides, or control peptides, were tested for their antigen dose response to the fluM58 peptide in a standard TNF bioassay. As shown in Figure 3, peptide P1S#10 competes HLA-A2 restricted presentation of fluM58, demonstrating that peptide P1S#10 binds HLA-A2.

Mice expressing the transgene for human HLA A2.1 were immunized as described by Theobald et al. (*Proc. Natl. Acad. Sci. USA 92*:11993-11997, 1995) with the following modifications. Mice were immunized with 62.5μg of P1S #10 and 120μg of an I-A<sup>b</sup> binding peptide derived from Hepatitis B Virus protein emulsified in incomplete Freund's adjuvant. Three weeks later these mice were sacrificed and single cell suspensions prepared using a nylon mesh. Cells were then resuspended at 6 x 10<sup>6</sup> cells/ml in complete media (as described above) and cultured in the presence of irradiated (3000 rads) P1S#10-pulsed (2μg/ml P1S#10 and 10mg/ml β2-microglobulin) LPS blasts (A2 transgenic spleens cells cultured in the presence of 7μg/ml dextran sulfate and 25μg/ml LPS for 3 days). Six days later cells (5 x 10<sup>5</sup>/ml) were restimulated with 2.5 x 10<sup>6</sup>/ml peptide-pulsed irradiated (20,000 rads) EL4A2Kb cells, as described above, and 3 x 10<sup>6</sup>/ml A2 transgenic spleen feeder cells. Cells were cultured in the presence of 20 U/ml IL-2. Cells were restimulated on a weekly

basis in preparation for cloning. After three rounds of *in vitro* stimulations, one line was generated that recognized P1S#10-pulsed Jurkat A2Kb targets and P501S-transduced Jurkat targets as shown in Figure 4.

A P1S#10-specific CTL line was cloned by limiting dilution analysis with peptide pulsed EL4 A2Kb tumor cells (1 x 10<sup>4</sup> cells/ well) as stimulators and A2 transgenic spleen cells as feeders (5 x 10<sup>5</sup> cells/ well) grown in the presence of 30U/ml IL-2. On day 14, cells were restimulated as before. On day 21, viable clones were isolated and maintained in culture. As shown in Figure 5, five of these clones demonstrated specific cytolytic reactivity against P501S-transduced Jurkat A2Kb targets. This data indicates that P1S#10 represents a naturally processed epitope of the P501S protein that is expressed in the context of the human HLA-A2.1 molecule.

## EXAMPLE 7 ABILITY OF HUMAN T CELLS TO RECOGNIZE PROSTATE TUMOR POLYPEPTIDES

This Example illustrates the ability of T cells specific for a prostate tumor polypeptide to recognize human tumor.

Human CD8<sup>+</sup> T cells were primed in vitro to the P2S-12 peptide (SEQ ID NO: 306) derived from P502S (also referred to as J1-17) using dendritic cells according to the protocol of Van Tsai et al. (Critical Reviews in Immunology 18:65-75, 1998). The resulting CD8+ T cell microcultures were tested for their ability to recognize the P2S-12 peptide presented by autologous fibroblasts or fibroblasts which were transduced to express the P502S gene in a γ-interferon ELISPOT assay (see Lalvani et al., J. Exp. Med. 186:859-865, 1997). Briefly, titrating numbers of T cells were assayed in duplicate on 104 fibroblasts in the presence of 3 μg/ml human β<sub>2</sub>-microglobulin and 1 μg/ml P2S-12 peptide or control E75 In addition, T cells were simultaneously assayed on autologous fibroblasts transduced with the P502S gene or as a control, fibroblasts transduced with HER-2/neu. Prior to the assay, the fibroblasts were treated with 10 ng/ml γ-interferon for 48 hours to upregulate class I MHC expression. One of the microcultures (#5) demonstrated strong recognition of both peptide pulsed fibroblasts as well as transduced fibroblasts in a γ-interferon ELISPOT assay. Figure 2A demonstrates that there was a strong increase in the number of y-interferon spots with increasing numbers of T cells on fibroblasts pulsed with the P2S-12 peptide (solid bars) but not with the control E75 peptide (open bars). This shows the ability of these T cells to specifically recognize the P2S-12 peptide. As shown in Figure 2B, this microculture also demonstrated an increase in the number of  $\gamma$ -interferon spots with increasing numbers of T

cells on fibroblasts transduced to express the P502S gene but not the HER-2/neu gene. These results provide additional confirmatory evidence that the P2S-12 peptide is a naturally processed epitope of the P502S protein. Furthermore, this also demonstrates that there exists in the human T cell repertoire, high affinity T cells which are capable of recognizing this epitope. These T cells should also be capable of recognizing human tumors which express the P502S gene.

## EXAMPLE 8 PRIMING OF CTL IN VIVO USING NAKED DNA IMMUNIZATION WITH A PROSTATE ANTIGEN

The prostate tumor antigen L1-12, as described above, is also referred to as P501S. HLA A2Kb Tg mice (provided by Dr L. Sherman, The Scripps Research Institute, La Jolla, CA) were immunized with 100 µg VR10132-P501S either intramuscularly or intradermally. The mice were immunized three times, with a two week interval between immunizations. Two weeks after the last immunization, immune spleen cells were cultured with Jurkat A2Kb-P501S transduced stimulator cells. CTL lines were stimulated weekly. After two weeks of *in vitro* stimulation, CTL activity was assessed against P501S transduced targets. Two out of 8 mice developed strong anti-P501S CTL responses. These results demonstrate that P501S contains at least one naturally processed A2-restricted CTL epitope.

### EXAMPLE 9

## GENERATION OF HUMAN CTL IN VITRO USING WHOLE GENE PRIMING AND STIMULATION TECHNIQUES WITH PROSTATE TUMOR ANTIGEN

Using *in vitro* whole-gene priming with P501S-retrovirally transduced autologous fibroblasts (see, for example, Yee et al, *The Journal of Immunology*, 157(9):4079-86, 1996), human CTL lines were derived that specifically recognize autologous fibroblasts transduced with P501S (also known as L1-12), as determined by interferon-γ ELISPOT analysis as described above. Using a panel of HLA-mismatched fibroblast lines transduced with P501S, these CTL lines were shown to be restricted HLA-A2 class I allele. Specifically, dendritic cells (DC) were differentiated from monocyte cultures derived from PBMC of normal human donors by growing for five days in RPMI medium containing 10% human serum, 50 ng/ml human GM-CSF and 30 ng/ml human IL-4. Following culture, DC were infected overnight with recombinant P501S vaccinia virus at a multiplicity of infection (M.O.I) of five, and matured overnight by the addition of 3 μg/ml CD40 ligand. Virus was inactivated by UV irradiation. CD8+ T cells were isolated using a magnetic bead system, and

priming cultures were initiated using standard culture techniques. Cultures were restimulated every 7-10 days using autologous primary fibroblasts retrovirally transduced with P501S. - Following four stimulation cycles, CD8+ T cell lines were identified that specifically produced interferon-γ when stimulated with P501S-transduced autologous fibroblasts. The P501S-specific activity could be sustained by the continued stimulation of the cultures with P501S-transduced fibroblasts in the presence of IL-15. A panel of HLA-mismatched fibroblast lines transduced with P501S were generated to define the restriction allele of the response. By measuring interferon-γ in an ELISPOT assay, the P501S specific response was shown to be restricted by HLA-A2. These results demonstrate that a CD8+ CTL response to P501S can be elicited.

#### **EXAMPLE 10**

### IDENTIFICATION OF A NATURALLY PROCESSED CTL EPITOPE CONTAINED WITHIN A PROSTATE TUMOR ANTIGEN

The 9-mer peptide p5 (SEQ ID NO: 338) was derived from the P703P antigen (also referred to as P20). The p5 peptide is immunogenic in human HLA-A2 donors and is a naturally processed epitope. Antigen specific CD8+ T cells can be primed following repeated in vitro stimulations with monocytes pulsed with p5 peptide. These CTL specifically recognize p5-pulsed target cells in both ELISPOT (as described above) and chromium release assays. Additionally, immunization of HLA-A2 transgenic mice with p5 leads to the generation of CTL lines which recognize a variety of P703P transduced target cells expressing either HLA-A2Kb or HLA-A2. Specifically, HLA-A2 transgenic mice were immunized subcutaneously in the footpad with 100 µg of p5 peptide together with 140 µg of hepatitis B virus core peptide (a Th peptide) in Freund's incomplete adjuvant. Three weeks post immunization, spleen cells from immunized mice were stimulated in vitro with peptide-pulsed LPS blasts. CTL activity was assessed by chromium release assay five days after primary in vitro stimulation. Retrovirally transduced cells expressing the control antigen P703P and HLA-A2Kb were used as targets. CTL lines that specifically recognized both p5-pulsed targets as well as P703P-expressing targets were identified.

Human in vitro priming experiments demonstrated that the p5 peptide is immunogenic in humans. Dendritic cells (DC) were differentiated from monocyte cultures derived from PBMC of normal human donors by culturing for five days in RPMI medium containing 10% human serum, 50 ng/ml human GM-CSF and 30 ng/ml human IL-4. Following culture, the DC were pulsed with p5 peptide and cultured with GM-CSF and IL-4 together with CD8+ T cell enriched PBMC. CTL lines were restimulated on a weekly basis

with p5-pulsed monocytes. Five to six weeks after initiation of the CTL cultures, CTL recognition of p5-pulsed target cells was demonstrated.

## EXAMPLE 11 EXPRESSION OF A BREAST TUMOR-DERIVED ANTIGEN IN PROSTATE

Isolation of the antigen B305D from breast tumor by differential display is described in US Patent Application No. 08/700,014, filed August 20, 1996. Several different splice forms of this antigen were isolated. The determined cDNA sequences for these splice forms are provided in SEQ ID NO: 366-375, with the predicted amino acid sequences corresponding to the sequences of SEQ ID NO: 292, 298 and 301-303 being provided in SEQ ID NO: 299-306, respectively.

The expression levels of B305D in a variety of tumor and normal tissues were examined by real time PCR and by Northern analysis. The results indicated that B305D is highly expressed in breast tumor, prostate tumor, normal prostate tumor and normal testes, with expression being low or undetectable in all other tissues examined (colon tumor, lung tumor, ovary tumor, and normal bone marrow, colon, kidney, liver, lung, ovary, skin, small intestine, stomach).

# EXAMPLE 12 ELICITATION OF PROSTATE TUMOR ANTIGEN-SPECIFIC CTL RESPONSES IN HUMAN BLOOD

This Example illustrates the ability of a prostate tumor antigen to elicit a CTL response in blood of normal humans.

Autologous dendritic cells (DC) were differentiated from monocyte cultures derived from PBMC of normal donors by growth for five days in RPMI medium containing 10% human serum, 50 ng/ml GMCSF and 30 ng/ml IL-4. Following culture, DC were infected overnight with recombinant P501S-expressing vaccinia virus at an M.O.I. of 5 and matured for 8 hours by the addition of 2 micrograms/ml CD40 ligand. Virus was inactivated by UV irradiation, CD8<sup>+</sup> cells were isolated by positive selection using magnetic beads, and priming cultures were initiated in 24-well plates. Following five stimulation cycles, CD8+ lines were identified that specifically produced interferon-gamma when stimulated with autologous P501S-transduced fibroblasts. The P501S-specific activity of cell line 3A-1 could be maintained following additional stimulation cycles on autologous B-LCL transduced with P501S. Line 3A-1 was shown to specifically recognize autologous B-LCL transduced to

express P501S, but not EGFP-transduced autologous B-LCL, as measured by cytotoxity assays (<sup>51</sup>Cr release) and interferon-gamma production (Interferon-gamma Elispot; see above and Lalvani et al., J. Exp. Med. 186:859-865, 1997). The results of these assays are presented in Figures 6A and 6B.

# EXAMPLE 13 IDENTIFICATION OF PROSTATE TUMOR ANTIGENS BY MICROARRAY ANALYSIS

This Example describes the isolation of certain prostate tumor polypeptides from a prostate tumor cDNA library.

A human prostate tumor cDNA expression library as described above was screened using microarray analysis to identify clones that display at least a three fold over-expression in prostate tumor and/or normal prostate tissue, as compared to non-prostate normal tissues (not including testis). 372 clones were identified, and 319 were successfully sequenced. Table I presents a summary of these clones, which are shown in SEQ ID NOs:385-400. Of these sequences SEQ ID NOs:386, 389, 390 and 392 correspond to novel genes, and SEQ ID NOs: 393 and 396 correspond to previously identified sequences. The others (SEQ ID NOs:385, 387, 388, 391, 394, 395 and 397-400) correspond to known sequences, as shown in Table I.

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Table I
Summary of Prostate Tumor Antigens

Known Genes	Previously identified Genes	Novel
		Genes
T-cell gamma chain	P504S	23379 (SEQ
·	·	ID NO:389)
Kallikrein	P1000C	23399 (SEQ
		ID NO:392)
Vector	P501S	23320 (SEQ
·		ID NO:386)
CGI-82 protein mRNA (23319; SEQ ID	P503S	23381 (SEQ
NO:385)		ID NO:390)
PSA	P510S	
Ald. 6 Dehyd.	P784P	
Lidital 2 dahadaaaaaa (2227), gpo yo	peace.	·
L-iditol-2 dehydrogenase (23376; SEQ ID NO:388)	P502S	
110.500)		
Ets transcription factor PDEF (22672; SEQ	P706P	
ID NO:398)	17001	*
hTGR (22678; SEQ ID NO:399)	19142.2, bangur.seq (22621; SEQ	
	ID NO:396)	
	Í	
KIAA0295(22685; SEQ ID NO:400)	5566.1 Wang(23404; SEQ ID	
	NO:393)	
• .		
Prostatic Acid Phosphatase(22655; SEQ ID	P712P	
NO:397)		·
·		
	·	

transglutaminase (22611; SEQ ID NO:395)	P778P
HDLBP (23508; SEQ ID NO:394)	
CGI-69 Protein(23367; SEQ ID NO:387)	
KIAA0122(23383; SEQ ID NO:391)	
TEEG	

CGI-82 showed 4.06 fold over-expression in prostate tissues as compared to other normal tissues tested. It was over-expressed in 43% of prostate tumors, 25% normal prostate, not detected in other normal tissues tested. L-iditol-2 dehydrogenase showed 4.94 fold over-expression in prostate tissues as compared to other normal tissues tested. It was over-expressed in 90% of prostate tumors, 100% of normal prostate, and not detected in other normal tissues tested. Ets transcription factor PDEF showed 5.55 fold over-expression in prostate tissues as compared to other normal tissues tested. It was over-expressed in 47% prostate tumors, 25% normal prostate and not detected in other normal tissues tested. hTGR1 showed 9.11 fold over-expression in prostate tissues as compared to other normal tissues tested. It was over-expressed in 63% of prostate tumors and is not detected in normal tissues tested including normal prostate. KIAA0295 showed 5.59 fold over-expression in prostate tissues as compared to other normal tissues tested. It was over-expressed in 47% of prostate tumors, low to undetectable in normal tissues tested including normal prostate tissues. Prostatic acid phosphatase showed 9.14 fold over-expression in prostate tissues as compared to other normal tissues tested. It was over-expressed in 67% of prostate tumors, 50% of normal prostate, and not detected in other normal tissues tested. Transglutaminase showed 14.84 fold over-expression in prostate tissues as compared to other normal tissues tested. It was over-expressed in 30% of prostate tumors, 50% of normal prostate, and is not detected in other normal tissues tested. High density lipoprotein binding protein (HDLBP) showed 28.06 fold over-expression in prostate tissues as compared to other normal tissues tested. It was over-expressed in 97% of prostate tumors, 75% of normal prostate, and is undetectable in all other normal tissues tested. CGI-69 showed 3.56 fold over-expression in prostate tissues as compared to other normal tissues tested. It is a low abundant gene, detected in more than 90% of prostate tumors, and in 75% normal prostate tissues. The expression of this gene in normal tissues was very low. KIAA0122 showed 4.24 fold over-expression in prostate

tissues as compared to other normal tissues tested. It was over-expressed in 57% of prostate tumors, it was undetectable in all normal tissues tested including normal prostate tissues. 19142.2 bangur showed 23.25 fold over-expression in prostate tissues as compared to other normal tissues tested. It was over-expressed in 97% of prostate tumors and 100% of normal prostate. It was undetectable in other normal tissues tested. 5566.1 Wang showed 3.31 fold over-expression in prostate tissues as compared to other normal tissues tested. It was overexpressed in 97% of prostate tumors, 75% normal prostate and was also over-expressed in normal bone marrow, pancreas, and activated PBMC. Novel clone 23379 showed 4.86 fold over-expression in prostate tissues as compared to other normal tissues tested. It was detectable in 97% of prostate tumors and 75% normal prostate and is undetectable in all other normal tissues tested. Novel clone 23399 showed 4.09 fold over-expression in prostate tissues as compared to other normal tissues tested. It was over-expressed in 27% of prostate tumors and was undetectable in all normal tissues tested including normal prostate tissues. Novel clone 23320 showed 3.15 fold over-expression in prostate tissues as compared to other normal tissues tested. It was detectable in all prostate tumors and 50% of normal prostate tissues. It was also expressed in normal colon and trachea. Other normal tissues do not express this gene at high level.

## EXAMPLE 14 IDENTIFICATION OF PROSTATE TUMOR ANTIGENS BY ELECTRONIC SUBTRACTION

This Example describes the use of an electronic subtraction technique to identify prostate tumor antigens.

Potential prostate-specific genes present in the GenBank human EST database were identified by electronic subtraction (similar to that described by Vasmatizis et al., *Proc. Natl. Acad. Sci. USA 95*:300-304, 1998). The sequences of EST clones (43,482) derived from various prostate libraries were obtained from the GenBank public human EST database. Each prostate EST sequence was used as a query sequence in a BLASTN (National Center for Biotechnology Information) search against the human EST database. All matches considered identical (length of matching sequence >100 base pairs, density of identical matches over this region > 70%) were grouped (aligned) together in a cluster. Clusters containing more than 200 ESTs were discarded since they probably represented repetitive elements or highly expressed genes such as those for ribosomal proteins. If two or more clusters shared common ESTs, those clusters were grouped together into a "supercluster," resulting in 4,345 prostate superclusters.

Records for the 479 human cDNA libraries represented in the GenBank release were downloaded to create a database of these cDNA library records. These 479 cDNA libraries were grouped into three groups, Plus (normal prostate and prostate tumor libraries, and breast cell lines, in which expression was desired), Minus (libraries from other normal adult tissues, in which expression was not desirable), and Other (fetal tissue, infant tissue, tissues found only in women, non-prostate tumors and cell lines other than prostate cell lines, in which expression was considered to be irrelevant). A summary of these library groups is presented in Table II.

<u>Table II</u>

<u>Prostate cDNA Libraries and ESTs</u>

Library	# of Libraries	# of ESTs
Plus	25	43,482
Normal	11	18,875
Tumor	′ 11	21,769
Cell lines	3	2,838
Minus	166	
Other	287	

Each supercluster was analyzed in terms of the ESTs within the supercluster. The tissue source of each EST clone was noted and used to classify the superclusters into four groups: Type 1- EST clones found in the Plus group libraries only; no expression detected in Minus or Other group libraries; Type 2- EST clones found in the Plus and Other group libraries only; no expression detected in the Minus group; Type 3- EST clones found in the Plus, Minus and Other group libraries, but the expression in the Plus group is higher than in either the Minus or Other groups; and Type 4- EST clones found in Plus, Minus and Other group libraries, but the expression in the Plus group is higher than the expression in the Minus group. This analysis identified 4,345 breast clusters (see Table III). From these clusters, 3,172 EST clones were ordered from Research Genetics, Inc., and were received as frozen glycerol stocks in 96-well plates.

<u>Table III</u> <u>Prostate Cluster Summary</u>

Туре	# of Superclusters	# of ESTs Ordered
1	688	677
2	2899	2484
3	85	11
4	673	0
Total	4345	3172

The inserts were PCR-amplified using amino-linked PCR primers for Synteni microarray analysis. When more than one PCR product was obtained for a particular clone, that PCR product was not used for expression analysis. In total, 2,528 clones from the electronic subtraction method were analyzed by microarray analysis to identify electronic subtraction breast clones that had high tumor vs. normal tissue mRNA. Such screens were performed using a Synteni (Palo Alto, CA) microarray, according to the manufacturer's instructions (and essentially as described by Schena et al., *Proc. Natl. Acad. Sci. USA 93*:10614-10619, 1996 and Heller et al., *Proc. Natl. Acad. Sci. USA 94*:2150-2155, 1997). Within these analyses, the clones were arrayed on the chip, which was then probed with fluorescent probes generated from normal and tumor prostate cDNA, as well as various other normal tissues. The slides were scanned and the fluorescence intensity was measured.

Clones with an expression ratio greater than 3 (i.e., the level in prostate tumor cDNA was at least three times the level in normal prostate cDNA) were identified as prostate tumor-specific sequences (Table IV). The sequences of these clones are provided in SEQ ID NOs:401-453, with certain novel sequences shown in SEQ ID NOs:407, 413, 416-419, 422, 426, 427 and 450.

<u>Table IV</u> <u>Prostate-tumor Specific Clones</u>

SEQ ID NO.	Sequence Designation	Comments
401	22545	previously identified P1000C
402	22547	previously identified P704P

400		
403	22548	known
: 404	22550	known
405	22551	PSA
406	22552	prostate secretory protein 94
407	22553	novel -
408	22558	previously identified P509S
409	22562	glandular kallikrein
410	22565	previously identified P1000C
411	22567	PAP
412	22568	B1006C (breast tumor antigen)
413	22570	novel
414	22571	PSA
415	22572	previously identified P706P
416	22573	novel
417	22574	novel
418	22575	novel
419	22580	novel
420	22581	PAP
421	22582	prostatic secretory protein 94
422	22583	novel
423	22584	prostatic secretory protein 94
424	22585	prostatic secretory protein 94
425	22586	known
426	22587	novel
427	22588	novel
428	22589	PAP
429	22590	known
430	22591	PSA
431	22592	known
432	22593	Previously identified P777P
433	22594	T cell receptor gamma chain
434	22595	Previously identified P705P
435	22596	Previously identified P707P
436	22847	PAP
437	22848	known
438	22849	prostatic secretory protein 57
· · · · · · · · · · · · · · · · · · ·	<del> </del>	

439	22851	PAP
440	22852	PAP
441	22853	PAP
442	22854	previously identified P509S
443	22855.	previously identified P705P
444	22856	previously identified P774P
445	22857	PSA
446	23601	previously identified P777P
447	23602	PSA
448	23605	PSA
449	23606	PSA
450	23612	novel
451	23614	PSA
452	23618	previously identified P1000C
453	23622	previously identified P705P

# EXAMPLE 15 FURTHER IDENTIFICATION OF PROSTATE TUMOR ANTIGENS BY MICROARRAY ANALYSIS

This Example describes the isolation of additional prostate tumor polypeptides from a prostate tumor cDNA library.

A human prostate tumor cDNA expression library as described above was screened using microarray analysis to identify clones that display at least a three fold over-expression in prostate tumor and/or normal prostate tissue, as compared to non-prostate normal tissues (not including testis). 142 clones were identified and sequenced. Certain of these clones are shown in SEQ ID NOs:454-467. Of these sequences SEQ ID NOs:459-461 correspond to novel genes. The others (SEQ ID NOs:454-458 and 461-467) correspond to known sequences.

## EXAMPLE 16 FURTHER CHARACTERIZATION OF PROSTATE TUMOR ANTIGEN P710P

This Example describes the full length cloning of P710P.

The prostate cDNA library described above was screened with the P710P fragment described above. One million colonies were plated on LB/Ampicillin plates. Nylon membrane filters were used to lift these colonies, and the cDNAs picked up by these filters were then denatured and cross-linked to the filters by UV light. The P710P fragment was radiolabeled and used to hybridize with the filters. Positive cDNA clones were selected and their cDNAs recovered and sequenced by an automatic ABI Sequencer. Four sequences were obtained, and are presented in SEQ ID NOs:468-471.

From the foregoing, it will be appreciated that, although specific embodiments of the invention have been described herein for the purposes of illustration, various modifications may be made without deviating from the spirit and scope of the invention. Accordingly, the present invention is not limited except as by the appended claims.

#### **CLAIMS**

- 1. An isolated polypeptide comprising at least an immunogenic portion of a prostate tumor protein, or a variant thereof, wherein the tumor protein comprises an amino acid sequence that is encoded by a polynucleotide sequence selected from the group consisting of:
- (a) sequences recited in any one of SEQ ID NOs:2, 3, 8-29, 41-45, 47-52, 54-65, 70, 73-74, 79, 81, 87, 90, 92, 93, 97, 103, 104, 107, 109-111, 115-160, 171, 173-175, 177, 181, 188, 191, 193, 194, 198, 203, 204, 207, 209, 220, 222-225, 227-305, 307-315, 326, 328, 330, 332, 334, 350-365, 381, 382, 384, 386, 389, 390, 392, 393, 396, 401, 402, 407, 408, 410, 413, 415-419, 422, 426, 427, 432, 434, 435, 442-444, 446, 450, 452, 453, 459-461, 468-471 or 472;
- (b) sequences that hybridize to any of the foregoing sequences under moderately stringent conditions; and
  - (c) complements of any of the sequence of (a) or (b).
- 2. An isolated polypeptide according to claim 1, wherein the polypeptide comprises an amino acid sequence that is encoded by a polynucleotide sequence recited in any one of SEQ ID NOs:2, 3, 8-29, 41-45, 47-52, 54-65, 70, 73-74, 79, 81, 87, 90, 92, 93, 97, 103, 104, 107, 109-111, 115-160, 171, 173-175, 177, 181, 188, 191, 193, 194, 198, 203, 204, 207, 209, 220, 222-225, 227-305, 307-315, 326, 328, 330, 332, 334, 350-365, 381, 382, 384, 386, 389, 390, 392, 393, 396, 401, 402, 407, 408, 410, 413, 415-419, 422, 426, 427, 432, 434, 435, 442-444, 446, 450, 452, 453, 459-461, 468-471 or 472, or a complement of any of the foregoing polynucleotide sequences.
- 3. An isolated polypeptide comprising a sequence recited in any one of SEQ ID NO: 108, 112, 113, 114, 172, 176, 178, 327, 329, 331, 339 and 383.
- 4. An isolated polynucleotide encoding at least 15 amino acid residues of a prostate tumor protein, or a variant thereof that differs in one or more substitutions, deletions, additions and/or insertions such that the ability of the variant to react with antigenspecific antisera is not substantially diminished, wherein the tumor protein comprises an amino acid sequence that is encoded by a polynucleotide comprising a sequence recited in any one of SEQ ID NOs:2, 3, 8-29, 41-45, 47-52, 54-65, 70, 73-74, 79, 81, 87, 90, 92, 93, 97, 103, 104, 107, 109-111, 115-160, 171, 173-175, 177, 181, 188, 191, 193, 194, 198, 203, 204, 207, 209, 220, 222-225, 227-305, 307-315, 326, 328, 330, 332, 334, 350-365, 381, 382, 384, 386, 389, 390, 392, 393, 396, 401, 402, 407, 408, 410, 413, 415-419, 422, 426, 427, 432, 434,

435, 442-444, 446, 450, 452, 453, 459-461, 468-471 or 472, or a complement of any of the foregoing sequences.

- 5. An isolated polynucleotide encoding a prostate tumor protein, or a variant thereof, wherein the tumor protein comprises an amino acid sequence that is encoded by a polynucleotide comprising a sequence recited in any one of SEQ ID NOs:2, 3, 8-29, 41-45, 47-52, 54-65, 70, 73-74, 79, 81, 87, 90, 92, 93, 97, 103, 104, 107, 109-111, 115-160, 171, 173-175, 177, 181, 188, 191, 193, 194, 198, 203, 204, 207, 209, 220, 222-225, 227-305, 307-315, 326, 328, 330, 332, 334, 350-365, 381, 382, 384, 386, 389, 390, 392, 393, 396, 401, 402, 407, 408, 410, 413, 415-419, 422, 426, 427, 432, 434, 435, 442-444, 446, 450, 452, 453, 459-461, 468-471 or 472, or a complement of any of the foregoing sequences.
- 6. An isolated polynucleotide comprising a sequence recited in any one of SEQ ID NOs:2, 3, 8-29, 41-45, 47-52, 54-65, 70, 73-74, 79, 81, 87, 90, 92, 93, 97, 103, 104, 107, 109-111, 115-160, 171, 173-175, 177, 181, 188, 191, 193, 194, 198, 203, 204, 207, 209, 220, 222-225, 227-305, 307-315, 326, 328, 330, 332, 334, 350-365, 381, 382, 384, 386, 389, 390, 392, 393, 396, 401, 402, 407, 408, 410, 413, 415-419, 422, 426, 427, 432, 434, 435, 442-444, 446, 450, 452, 453, 459-461, 468-471 or 472.
- 7. An isolated polynucleotide comprising a sequence that hybridizes, under moderately stringent conditions, to a sequence recited in any one of SEQ ID NOs:2, 3, 8-29, 41-45, 47-52, 54-65, 70, 73-74, 79, 81, 87, 90, 92, 93, 97, 103, 104, 107, 109-111, 115-160, 171, 173-175, 177, 181, 188, 191, 193, 194, 198, 203, 204, 207, 209, 220, 222-225, 227-305, 307-315, 326, 328, 330, 332, 334, 350-365, 381, 382, 384, 386, 389, 390, 392, 393, 396, 401, 402, 407, 408, 410, 413, 415-419, 422, 426, 427, 432, 434, 435, 442-444, 446, 450, 452, 453, 459-461, 468-471 or 472.
- 8. An isolated polynucleotide complementary to a polynucleotide according to any one of claims 4-7.
- 9. An expression vector comprising a polynucleotide according to any one of claims 4-7.
- 10. A host cell transformed or transfected with an expression vector according to claim 9.
  - 11. An expression vector comprising a polynucleotide according claim 8.

- 12. A host cell transformed or transfected with an expression vector according to claim 11.
- 13. A pharmaceutical composition comprising a polypeptide according to claim 1, in combination with a physiologically acceptable carrier.
- 14. A vaccine comprising a polypeptide according to claim 1, in combination with a non-specific immune response enhancer.
- 15. A vaccine according to claim 14, wherein the non-specific immune response enhancer is an adjuvant.
- 16. A vaccine according to claim 14, wherein the non-specific immune response enhancer induces a predominantly Type I response.
- 17. A pharmaceutical composition comprising a polynucleotide according to claim 4, in combination with a physiologically acceptable carrier.
- 18. A vaccine comprising a polynucleotide according to claim 4, in combination with a non-specific immune response enhancer.
- 19. A vaccine according to claim 18, wherein the non-specific immune response enhancer is an adjuvant.
- 20. A vaccine according to claim 18, wherein the non-specific immune response enhancer induces a predominantly Type I response.
- 21. An isolated antibody, or antigen-binding fragment thereof, that specifically binds to a prostate tumor protein that comprises an amino acid sequence that is encoded by a polynucleotide sequence recited in any one of SEQ ID NOs:2, 3, 8-29, 41-45, 47-52, 54-65, 70, 73-74, 79, 81, 87, 90, 92, 93, 97, 103, 104, 107, 109-111, 115-160, 171, 173-175, 177, 181, 188, 191, 193, 194, 198, 203, 204, 207, 209, 220, 222-225, 227-305, 307-315, 326, 328, 330, 332, 334, 350-365, 381, 382, 384, 386, 389, 390, 392, 393, 396, 401, 402, 407, 408, 410, 413, 415-419, 422, 426, 427, 432, 434, 435, 442-444, 446, 450, 452, 453, 459-461, 468-471 or 472 or a complement of any of the foregoing polynucleotide sequences.

- 22. A pharmaceutical composition comprising an antibody or fragment thereof according to claim 18, in combination with a physiologically acceptable carrier.
- 23. A pharmaceutical composition comprising an antigen-presenting cell that expresses a polypeptide according to claim 1, in combination with a pharmaceutically acceptable carrier or excipient.
- 24. A pharmaceutical composition according to claim 23, wherein the antigen presenting cell is a dendritic cell or a macrophage.
- 25. A vaccine comprising an antigen-presenting cell that expresses a polypeptide according to claim 1, in combination with a non-specific immune response enhancer.
- 26. A vaccine according to claim 25, wherein the non-specific immune response enhancer is an adjuvant.
- 27. A vaccine according to claim 25, wherein the non-specific immune response enhancer induces a predominantly Type I response.
- 28. A vaccine according to claim 25, wherein the antigen-presenting cell is a dendritic cell.
- 29. A method for inhibiting the development of a cancer in a patient, comprising administering to a patient an effective amount of a polypeptide according to claim 1, and thereby inhibiting the development of a cancer in the patient.
- 30. A method for inhibiting the development of a cancer in a patient, comprising administering to a patient an effective amount of a polynucleotide according to claim 4, and thereby inhibiting the development of a cancer in the patient.
- 31. A method for inhibiting the development of a cancer in a patient, comprising administering to a patient an effective amount of an antibody or antigen-binding fragment thereof according to claim 21, and thereby inhibiting the development of a cancer in the patient.

- 32. A method for inhibiting the development of a cancer in a patient, comprising administering to a patient an effective amount of an antigen-presenting cell that expresses a polypeptide according to claim 1, and thereby inhibiting the development of a cancer in the patient.
- 33. A method according to claim 32, wherein the antigen-presenting cell is a dendritic cell.
- 34. A method according to any one of claims 29-32, wherein the cancer is prostate cancer.
- 35. A fusion protein comprising at least one polypeptide according to claim 1.
- 36. A fusion protein according to claim 35, wherein the fusion protein comprises an expression enhancer that increases expression of the fusion protein in a host cell transfected with a polynucleotide encoding the fusion protein.
- 37. A fusion protein according to claim 35, wherein the fusion protein comprises a T helper epitope that is not present within the polypeptide of claim 1.
- 38. A fusion protein according to claim 35, wherein the fusion protein comprises an affinity tag.
- 39. An isolated polynucleotide encoding a fusion protein according to claim 35.
- 40. A pharmaceutical composition comprising a fusion protein according to claim 32, in combination with a physiologically acceptable carrier.
- 41. A vaccine comprising a fusion protein according to claim 35, in combination with a non-specific immune response enhancer.
- 42. A vaccine according to claim 41, wherein the non-specific immune response enhancer is an adjuvant.

- 43. A vaccine according to claim 41, wherein the non-specific immune response enhancer induces a predominantly Type I response.
- 44. A pharmaceutical composition comprising a polynucleotide according to claim 40, in combination with a physiologically acceptable carrier.
- 45. A vaccine comprising a polynucleotide according to claim 40, in combination with a non-specific immune response enhancer.
- 46. A vaccine according to claim 45, wherein the non-specific immune response enhancer is an adjuvant.
- 47. A vaccine according to claim 45, wherein the non-specific immune response enhancer induces a predominantly Type I response.
- 48. A method for inhibiting the development of a cancer in a patient, comprising administering to a patient an effective amount of a pharmaceutical composition according to claim 40 or claim 44.
- 49. A method for inhibiting the development of a cancer in a patient, comprising administering to a patient an effective amount of a vaccine according to claim 41 or claim 45.
- 50. A method for removing tumor cells from a biological sample, comprising contacting a biological sample with T cells that specifically react with a prostate tumor protein, wherein the tumor protein comprises an amino acid sequence that is encoded by a polynucleotide sequence selected from the group consisting of:
- (i) polynucleotides recited in any one of SEQ ID NOs:1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382 or 384-472; and
  - (ii) complements of the foregoing polynucleotides;

wherein the step of contacting is performed under conditions and for a time sufficient to permit the removal of cells expressing the prostate tumor protein from the sample.

51. A method according to claim 50, wherein the biological sample is blood or a fraction thereof.

- 52. A method for inhibiting the development of a cancer in a patient, comprising administering to a patient a biological sample treated according to the method of claim 50.
- 53. A method for stimulating and/or expanding T cells specific for a prostate tumor protein, comprising contacting T cells with one or more of:
  - (i) a polypeptide according to claim 1;
- (ii) a polypeptide encoded by a polynucleotide comprising a sequence provided in any one of SEQ ID NOs:1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382 or 384-472;
  - (iii) a polynucleotide encoding a polypeptide of (i) or (ii); and/or
- (iv) an antigen presenting cell that expresses a polypeptide of (i) or (ii); under conditions and for a time sufficient to permit the stimulation and/or expansion of T cells.
- 54. An isolated T cell population, comprising T cells prepared according to the method of claim 53.
- 55. A method for inhibiting the development of a cancer in a patient, comprising administering to a patient an effective amount of a T cell population according to claim 54.
- 56. A method for inhibiting the development of a cancer in a patient, comprising the steps of:
- (a) incubating CD4<sup>+</sup> and/or CD8+ T cells isolated from a patient with at least one component selected from the group consisting of:
  - (i) a polypeptide according to claim 1;
- (ii) a polypeptide encoded by a polynucleotide comprising a sequence of any one of SEQ ID NOs:1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382 or 384-472;
  - (iii) a polynucleotide encoding a polypeptide of (i) or (ii); or
- (iv) an antigen-presenting cell that expresses a polypeptide of (i) or (ii);

such that T cells proliferate; and

(b) administering to the patient an effective amount of the proliferated T cells, and thereby inhibiting the development of a cancer in the patient.

- 57. A method for inhibiting the development of a cancer in a patient, comprising the steps of:
- (a) incubating CD4<sup>+</sup> and/or CD8+ T cells isolated from a patient with at least one component selected from the group consisting of:
  - (i) a polypeptide according to claim 1;
- (ii) a polypeptide encoded by a polynucleotide comprising a sequence of any one of SEQ ID NOs: 1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382 or 384-472;
  - (iii) a polynucleotide encoding a polypeptide of (i) or (ii); or
- (iv) an antigen-presenting cell that expresses a polypeptide of (i) or(ii);

such that T cells proliferate;

- (b) cloning at least one proliferated cell; and
- (c) administering to the patient an effective amount of the cloned T cells, and thereby inhibiting the development of a cancer in the patient.
- 58. A method for determining the presence or absence of a cancer in a patient, comprising the steps of:
- (a) contacting a biological sample obtained from a patient with a binding agent that binds to a prostate tumor protein, wherein the tumor protein comprises an amino acid sequence that is encoded by a polynucleotide sequence selected from the group consisting of:
- (i) polynucleotides recited in any one of SEQ ID NOs:1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382 or 384-472; and
  - (ii) complements of the foregoing polynucleotides;
- (b) detecting in the sample an amount of polypeptide that binds to the binding agent; and
- (c) comparing the amount of polypeptide to a predetermined cut-off value, and therefrom determining the presence or absence of a cancer in the patient.
- 59. A method according to claim 58, wherein the binding agent is an antibody.
- 60. A method according to claim 59, wherein the antibody is a monoclonal antibody.

- 61. A method according to claim 58, wherein the cancer is prostate cancer.
- 62. A method for monitoring the progression of a cancer in a patient, comprising the steps of:
- (a) contacting a biological sample obtained from a patient at a first point in time with a binding agent that binds to a prostate tumor protein, wherein the tumor protein comprises an amino acid sequence that is encoded by a polynucleotide sequence recited in any one of SEQ ID NOs:1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382 or 384-472, or a complement of any of the foregoing polynucleotides;
- (b) detecting in the sample an amount of polypeptide that binds to the binding agent;
- (c) repeating steps (a) and (b) using a biological sample obtained from the patient at a subsequent point in time; and
- (d) comparing the amount of polypeptide detected in step (c) to the amount detected in step (b) and therefrom monitoring the progression of the cancer in the patient.
- 63. A method according to claim 62, wherein the binding agent is an antibody.
- 64. A method according to claim 63, wherein the antibody is a monoclonal antibody.
- 65. A method according to claim 62, wherein the cancer is a prostate cancer.
- 66. A method for determining the presence or absence of a cancer in a patient, comprising the steps of:
- (a) contacting a biological sample obtained from a patient with an oligonucleotide that hybridizes to a polynucleotide that encodes a prostate tumor protein, wherein the tumor protein comprises an amino acid sequence that is encoded by a polynucleotide sequence recited in any one of SEQ ID NOs:1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382 or 384-472, or a complement of any of the foregoing polynucleotides;
- (b) detecting in the sample an amount of a polynucleotide that hybridizes to the oligonucleotide; and

- (c) comparing the amount of polynucleotide that hybridizes to the oligonucleotide to a predetermined cut-off value, and therefrom determining the presence or absence of a cancer in the patient.
- 67. A method according to claim 66, wherein the amount of polynucleotide that hybridizes to the oligonucleotide is determined using a polymerase chain reaction.
- 68. A method according to claim 66, wherein the amount of polynucleotide that hybridizes to the oligonucleotide is determined using a hybridization assay.
- 69. A method for monitoring the progression of a cancer in a patient, comprising the steps of:
- (a) contacting a biological sample obtained from a patient with an oligonucleotide that hybridizes to a polynucleotide that encodes a prostate tumor protein, wherein the tumor protein comprises an amino acid sequence that is encoded by a polynucleotide sequence recited in any one of SEQ ID NOs:1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382 or 384-472, or a complement of any of the foregoing polynucleotides;
- (b) detecting in the sample an amount of a polynucleotide that hybridizes to the oligonucleotide;
- (c) repeating steps (a) and (b) using a biological sample obtained from the patient at a subsequent point in time; and
- (d) comparing the amount of polynucleotide detected in step (c) to the amount detected in step (b) and therefrom monitoring the progression of the cancer in the patient.
- 70. A method according to claim 69, wherein the amount of polynucleotide that hybridizes to the oligonucleotide is determined using a polymerase chain reaction.
- 71. A method according to claim 69, wherein the amount of polynucleotide that hybridizes to the oligonucleotide is determined using a hybridization assay.
  - 72. A diagnostic kit, comprising:
  - (a) one or more antibodies according to claim 21; and
  - (b) a detection reagent comprising a reporter group.

- 73. A kit according to claim 72, wherein the antibodies are immobilized on a solid support.
- 74. A kit according to claim 73, wherein the solid support comprises nitrocellulose, latex or a plastic material.
- 75. A kit according to claim 72, wherein the detection reagent comprises an anti-immunoglobulin, protein G, protein A or lectin.
- 76. A kit according to claim 72, wherein the reporter group is selected from the group consisting of radioisotopes, fluorescent groups, luminescent groups, enzymes, biotin and dye particles.
- 77. An oligonucleotide comprising 10 to 40 nucleotides that hybridize under moderately stringent conditions to a polynucleotide that encodes a prostate tumor protein, wherein the tumor protein comprises an amino acid sequence that is encoded by a polynucleotide sequence recited in any one of SEQ ID NOs:2, 3, 8-29, 41-45, 47-52, 54-65, 70, 73-74, 79, 81, 87, 90, 92, 93, 97, 103, 104, 107, 109-111, 115-160, 171, 173-175, 177, 181, 188, 191, 193, 194, 198, 203, 204, 207, 209, 220, 222-225, 227-305, 307-315, 326, 328, 330, 332, 334, 350-365, 381, 382, 384, 386, 389, 390, 392, 393, 396, 401, 402, 407, 408, 410, 413, 415-419, 422, 426, 427, 432, 434, 435, 442-444, 446, 450, 452, 453, 459-461, 468-471 or 472, or a complement of any of the foregoing polynucleotides.
- 78. A oligonucleotide according to claim 77, wherein the oligonucleotide comprises 10-40 nucleotides recited in any one of SEQ ID NOs:2, 3, 8-29, 41-45, 47-52, 54-65, 70, 73-74, 79, 81, 87, 90, 92, 93, 97, 103, 104, 107, 109-111, 115-160, 171, 173-175, 177, 181, 188, 191, 193, 194, 198, 203, 204, 207, 209, 220, 222-225, 227-305, 307-315, 326, 328, 330, 332, 334, 350-365, 381, 382, 384, 386, 389, 390, 392, 393, 396, 401, 402, 407, 408, 410, 413, 415-419, 422, 426, 427, 432, 434, 435, 442-444, 446, 450, 452, 453, 459-461, 468-471 or 472.
  - 79. A diagnostic kit, comprising:
  - (a) an oligonucleotide according to claim 77; and
- (b) a diagnostic reagent for use in a polymerase chain reaction or hybridization assay.

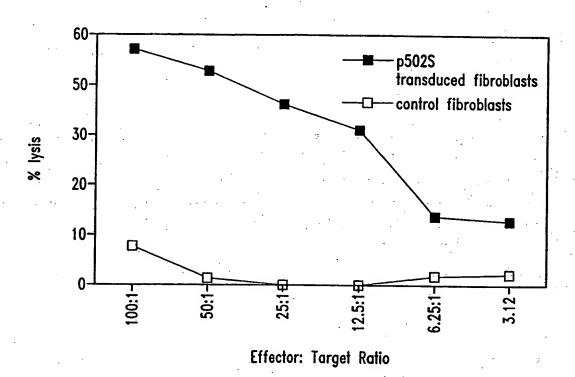


Fig. 1

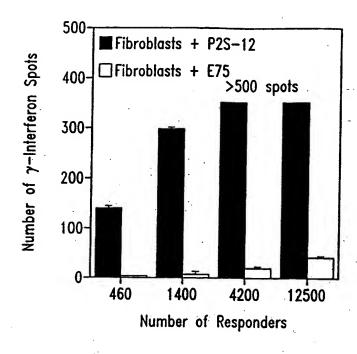


Fig. 2A

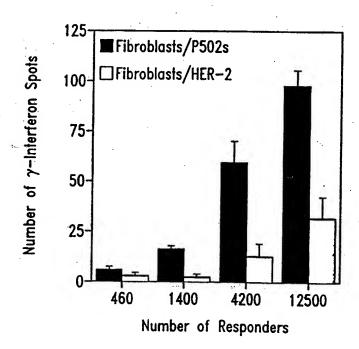


Fig. 2B

SUBSTITUTE SHEET (RULE 26)

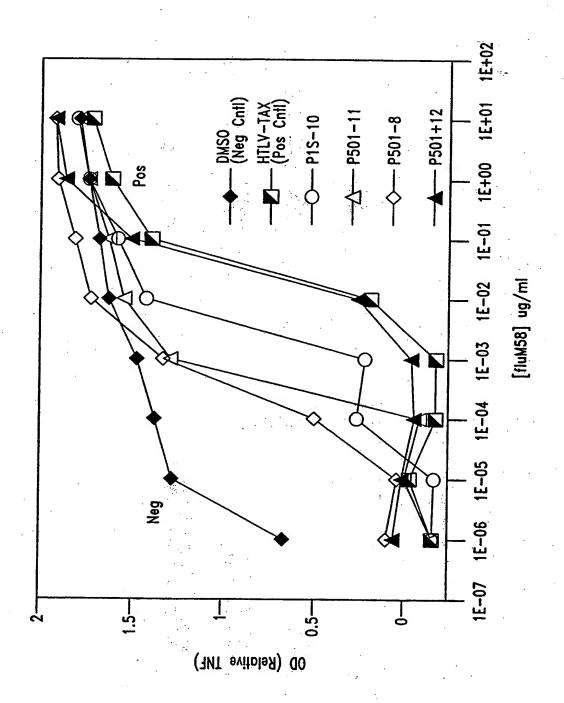


Fig. 3

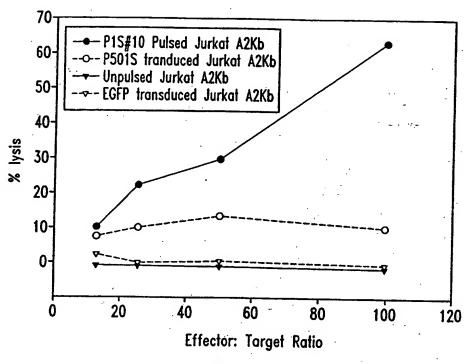
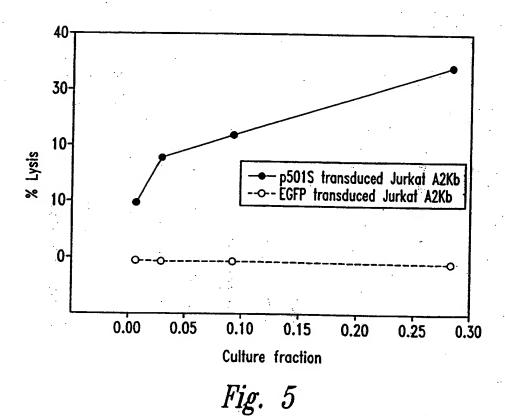
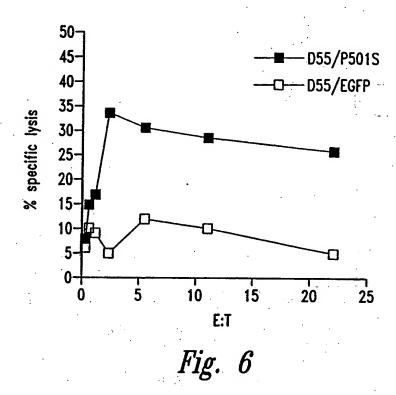
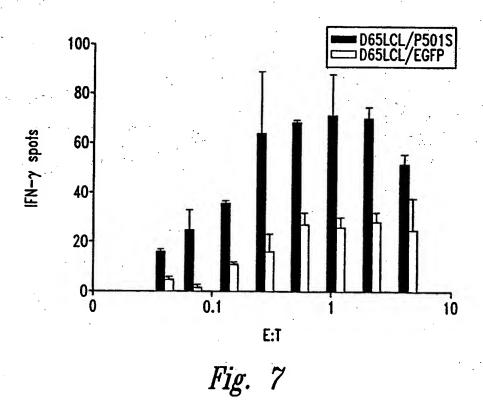


Fig. 4



SUBSTITUTE SHEET (RULE 26)





SUBSTITUTE SHEET (RULE 26)

120

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DHENOOD AND MARRIADE

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tegeteattg atcetngene eeggtetteg getgeggnga aeggtteaet ceteaaagge
                                                                        780
ggtntnccgg ttatccccaa acnggggata cccnga
                                                                        816
      <210> 3
      <211> 773
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(773)
      \langle 223 \rangle n = A,T,C or G
      <400> 3
cttttgaaag aagggatggc tggggtgttt aacagcagag gtgcagggcg ggggctcacg
                                                                        60
tectgetect caetggtgat aaacgagece egtteettgt tgtgateatg atgaacaace
                                                                       120
tectcaaaag teagaacegg agteacaeag geatetgtge egteaaagat ttgacaceae
                                                                       180
tetgeetteg tettettige aaatacatet geaaacttet tetteattie tggecaatea
                                                                       240
tccatgctca tctgattggg aagttcatca gactttagtc canntccttt gatcagcagc
                                                                       300
tegtagaact ggggttetat tgeteeaaca gecatgaatt ceceatetge tgteetgtaa
                                                                       360
gtcgtataga aaggtgctcc accatccaac atgttctgtc ctcgaggggg ggcccggtac
                                                                       420
ccaattegee etatantgag tegtattaeg egegeteact ggeegtegtt ttacaaegte
                                                                       480
gtgactggga aaaccctggg cgttaccaac ttaatcgcct tgcagcacat ccccctttcg
                                                                       540
ccagctgggc gtaatancga aaaggcccgc accgatcgcc cttccaacag ttgcgcacct
                                                                       600
gaatgggnaa atgggacccc cctgttaccg cgcattnaac ccccgcnggg tttngttgtt
                                                                       660
accccaent nnacegetta caetttgeca gegeettane geeegeteee ttteneettt
                                                                       720
ettecettee titeneneen ettteeeceg gggttteece enteaaacce ena
      <210> 4
      <211> 828
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(828)
      <223> n = A,T,C or G
      <400> 4 ·
cctcctgagt cctactgacc tgtgctttct ggtgtggagt ccagggctgc taggaaaagg
                                                                        60
aatgggcaga cacaggtgta tgccaatgtt tctgaaatgg gtataatttc gtcctctct
                                                                       120
teggaacact ggetgtetet gaagacttet egeteagttt cagtgaggae acacacaaag
                                                                       180
acgtgggtga ccatgttgtt tgtggggtgc agagatggga ggggtggggc ccaccctgga
                                                                       240
agagtggaca gtgacacaag gtggacactc tctacagatc actgaggata agctggagcc
                                                                       300
acaatgcatg aggcacacac acagcaagga tgacnctgta aacatagccc acgctgtcct
                                                                       360
```

```
gngggcactg ggaagcctan atnaggccgt gagcanaaag aaggggagga tccactagtt
                                                                        420
 ctanagegge egecacegeg gtgganetee anettttgtt eeetttagtg agggttaatt
                                                                        480
 gcgcgcttgg cntaatcatg gtcatanctn tttcctgtgt gaaattgtta tccgctcaca
                                                                        540
 attecacaca acatacgane eggaaacata aantgtaaac etggggtgee taatgantga
                                                                        600
 ctaactcaca ttaattgcgt tgcgctcact gcccgctttc caatcnggaa acctgtcttg
                                                                       660
 concttgcat thatgaatch gccaaccccc ggggaaaagc gtttgcgttt tgggcgctct
                                                                       720
 teegetteet eneteantta nteectnene teggteatte eggetgenge aaaceggtte
                                                                       780
 accnecteea aagggggtat teeggtttee cenaateegg ggananee
                                                                       828
      <210> 5
      <211> 834
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(834)
      <223> n = A,T,C or G
      <400> 5
ttttttttt tttttactga tagatggaat ttattaagct tttcacatgt gatagcacat
                                                                        60
agttttaatt gcatccaaag tactaacaaa aactctagca atcaagaatg gcagcatgtt
                                                                       120
attttataac aatcaacacc tgtggctttt aaaatttggt tttcataaga taatttatac
                                                                       180
tgaagtaaat ctagccatgc ttttaaaaaa tgctttaggt cactccaagc ttggcagtta
                                                                       240
acatttggca taaacaataa taaaacaatc acaatttaat aaataacaaa tacaacattg
                                                                       300
taggccataa tcatatacag tataaggaaa aggtggtagt gttgagtaag cagttattag
                                                                       360
aatagaatac cttggcctct atgcaaatat gtctagacac tttgattcac tcagcctga
                                                                       420
catteagttt tcaaagtagg agacaggttc tacagtatca ttttacagtt tccaacacat
                                                                       480
tgaaaacaag tagaaaatga tgagttgatt tttattaatg cattacatcc tcaagagtta
                                                                       540
tcaccaaccc ctcagttata aaaaattttc aagttatatt agtcatataa cttggtgtgc
                                                                       600
ttattttaaa ttagtgctaa atggattaag tgaagacaac aatggtcccc taatgtgatt
                                                                       660
gatattggtc atttttacca gcttctaaat ctnaactttc aggcttttga actggaacat
                                                                       720
tgnatnacag tgttccanag ttncaaccta ctggaacatt acagtgtgct tgattcaaaa
                                                                       780
tgttattttg ttaaaaatta aattttaacc tggtggaaaa ataatttgaa atna
      <210> 6
      <211> 818
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(818)
      <223> n = A,T,C or G
      <400> 6
ttttttttt tttttttt aagaccctca tcaatagatg gagacataca gaaatagtca
                                                                       60
aaccacatct acaaaatgcc agtatcaggc ggcggcttcg aagccaaagt gatgtttgga
                                                                      120
tgtaaagtga aatattagtt ggcggatgaa gcagatagtg aggaaagttg agccaataat
                                                                      180
gacgtgaagt ccgtggaagc ctgtggctac aaaaaatgtt gagccgtaga tgccgtcgga
                                                                      240
aatggtgaag ggagactcga agtactctga ggcttgtagg agggtaaaat agagacccag
                                                                      300
taaaattgta ataagcagtg cttgaattat ttggtttcgg ttgtttcta ttagactatg
                                                                      360
gtgagctcag gtgattgata ctcctgatgc gagtaatacg gatgtgttta ggagtgggac
                                                                      420
ttctagggga tttagcgggg tgatgcctgt tgggggccag tgccctccta gttggggggt
                                                                      480
aggggctagg ctggagtggt aaaaggctca gaaaaatcct gcgaagaaaa aaacttctga
```

```
ggtaataaat aggattatcc cgtatcgaag gcctttttgg acaggtggtg tgtggtgcc
                                                                       600
ttggtatgtg ctttctcgtg ttacatcgcg ccatcattgg tatatggtta gtgtgttggg
                                                                       660
ttantanggc ctantatgaa gaacttttgg antggaatta aatcaatngc ttggccggaa
                                                                       720
gtcattanga nggctnaaaa ggccctgtta ngggtctggg ctnggtttta cccnacccat
                                                                       780 -
ggaatnenee eeeeggaena ntgnateeet attettaa
                                                                       818
      <210> 7
      <211> 817
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1) ... (817)
      \langle 223 \rangle n = A,T,C or G
      <400> 7
tttttttttt ttttttttt tggctctaga gggggtagag ggggtgctat agggtaaata
                                                                        60
cgggccctat ttcaaagatt tttaggggaa ttaattctag gacgatgggt atgaaactgt
                                                                       120
ggtttgctcc acagatttca gagcattgac cgtagtatac ccccggtcgt gtagcggtga
                                                                       180
aagtggtttg gtttagacgt ccgggaattg catctgtttt taagcctaat gtggggacag
ctcatgagtg caagacgtct tgtgatgtaa ttattatacn aatgggggct tcaatcggga
                                                                       300
gtactactcg attgtcaacg tcaaggagtc gcaggtcgcc tggttctagg aataatgggg
                                                                       360
gaagtatgta ggaattgaag attaatccgc cgtagtcggt gttctcctag gttcaatacc
                                                                       420
attggtggcc aattgatttg atggtaaggg gagggatcgt tgaactcgtc tgttatgtaa
                                                                       480
aggatneett ngggatggga aggenatnaa ggaetangga tnaatggegg geangatatt
                                                                       540
tcaaacngtc tctanttcct gaaacgtctg aaatgttaat aanaattaan tttngttatt
                                                                       600
gaatnttnng gaaaagggct tacaggacta gaaaccaaat angaaaanta atnntaangg
                                                                       660
cnttatentn aaaggtnata accnetecta tnateceace caatngnatt ecceaenenn
                                                                       720
achattggat nececantte canaaangge enceceegg tgnanneene ettttgttee
                                                                       780
cttnantgan ggttattene eeetngentt atcance
                                                                       817
      <210> 8
      <211> 799
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(799)
      <223> n = A,T,C or G
      <400> 8
catttccggg tttactttct aaggaaagcc gagcggaagc tgctaacgtg ggaatcggtg
                                                                        60.
cataaggaga actttctgct ggcacgcgct agggacaagc gggagagcga ctccgagcgt
                                                                       120
ctgaagcgca cgtcccagaa ggtggacttg gcactgaaac agctgggaca catccgcgag
                                                                       180
tacgaacage geetgaaagt getggagegg gaggteeage agtgtageeg egteetgggg
                                                                       240
tgggtggccg angectgane egetetgeet tgetgeeece angtgggeeg eeaceeeetg
                                                                       300
acctgcctgg gtccaaacac tgagccctgc tggcggactt caagganaac ccccacangg
                                                                       360
ggattttgct cctanantaa ggctcatctg ggcctcggcc ccccacctg gttggccttg
                                                                       420
tetttgangt gagececatg tecatetggg ceaetgteng gaceaeettt ngggagtgtt
                                                                       480
ctccttacaa ccacannatg cccggctcct cccggaaacc antcccancc tgngaaggat
                                                                       540
caagneetgn atceactnnt netanaaccg geeneeneeg engtggaacc encettntgt
                                                                       600
teettttent tnagggttaa tnnegeettg geettneean ngteetnene ntttteennt
                                                                       660
```

gttnaaattg ttangeneee neennteeen ennennenan eeegaeeenn annttnnann

nectgggggt neennengat tgaccennee neeetntant tgenttnggg nnenntgeee

```
ctttccctct nggganncg
                                                                         799
       <210> 9
       <211> 801
       <212> DNA
       <213> Homo sapien
       <220>
       <221> misc_feature
       <222> (1)...(801)
       \langle 223 \rangle n = A,T,C or G
       <400> 9
 acgcettgat ceteccagge tgggaetggt tetgggagga geegggeatg etgtggtttg
                                                                         60
 taangatgac actcccaaag gtggtcctga cagtggccca gatggacatg gggctcacct
                                                                        120
caaggacaag gccaccaggt gcgggggccg aagcccacat gatccttact ctatgagcaa
                                                                        180
aatcccctgt gggggcttct ccttgaagtc cgccancagg gctcagtctt tggacccang
                                                                        240
caggicatgg ggitgingne caactggggg ceneaacgea aaanggenea gggeetengn
                                                                        300
cacccatcce angacgegge tacactnetg gacetecene tecaccaett teatgegetg
                                                                        360
ttentaceeg egnatnigie ecanetitt engigeenae tecanetiet nggaegigeg
                                                                        420
ctacatacge eeggantene netecegett tgteectate caegtneean caacagatt
                                                                        480
encentantg cacenattee caenttinne agnitteene nnegngette ettitaaaag
                                                                        540
ggttganccc cggaaaatnc cccaaagggg gggggccngg tacccaactn cccctnata
                                                                        600
gctgaantcc ccatnaccnn gnctcnatgg ancentcent tttaannacn ttctnaactt
                                                                        660
gggaanance etegneentn ecceenttaa teceneettg enangment ecceenntee
                                                                        720
ncccnnntng gentntnann enaaaaagge cennnancaa teteetnnen ceteantteg
                                                                        780
ccancecteg aaateggeen e
                                                                        801
      <210> 10
      <211> 789
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(789)
      <223> n = A, T, C or G
      <400> 10
cagtetaint ggccagtgtg gcagetttee etgtggetge eggtgeeaca tgcctgteec
                                                                         60
acagtgtggc cgtggtgaca gcttcagccg ccctcaccgg gttcaccttc tcagccctgc
                                                                       120
agatectgee ctacacactg geetecetet accaceggga gaageaggtg tteetgeeca
                                                                       180
aataccgagg ggacactgga ggtgctagca gtgaggacag cctgatgacc agcttcctgc
                                                                       240
caggecetaa geetggaget eeetteeeta atggacaegt gggtgetgga ggcagtggee
                                                                       300
tgctcccacc tccacccgcg ctctgcgggg cctctgcctg tgatgtctcc gtacgtgtgg
                                                                       360
tggtgggtga gcccaccgan gccagggtgg ttccgggccg gggcatctgc ctggacctcg
                                                                       420
ccatcctgga tagtgcttcc tgctgtccca ngtggcccca tccctgttta tgggctccat
                                                                       480
tgtccagctc agccagtctg tcactgccta tatggtgtct gccgcaggcc tgggtctggt
                                                                       540
cccatttact ttgctacaca ggtantattt gacaagaacg anttggccaa atactcagcg
                                                                       600
ttaaaaaaatt ccagcaacat tgggggtgga aggcctgcct cactgggtcc aactccccgc
                                                                       660
tectgttaac eccatgggge tgeeggettg geegecaatt tetgttgetg ecaaantnat
                                                                       720
gtggctctct gctgccacct gttgctggct gaagtgcnta cngcncanct nggggggtng
                                                                       780
ggngttccc
                                                                       789
```

<212> DNA

<213> Homo sapien

```
<210> 11
      <211> 772
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc feature
      <222> (1)...(772)
      \langle 223 \rangle n = A,T,C or G
      <400> 11
cccaccctac ccaaatatta gacaccaaca cagaaaagct agcaatggat tcccttctac
                                                                        60
tttgttaaat aaataagtta aatatttaaa tgcctgtgtc tctgtgatgg caacagaagg
                                                                       120
accaacaggc cacatcctga taaaaggtaa gaggggggtg gatcagcaaa aagacagtgc
                                                                       180
tgtgggctga ggggacctgg ttcttgtgtg ttgcccctca ggactcttcc cctacaaata
                                                                       240
actttcatat gttcaaatcc catggaggag tgtttcatcc tagaaactcc catgcaagag
                                                                       300
ctacattaaa cgaagctgca ggttaagggg cttanagatg ggaaaccagg tgactgagtt
                                                                       360
tattcagete ecaaaaacee ttetetaggt gtgteteaac taggaggeta getgttaace
                                                                       420
ctgagcctgg gtaatccacc tgcagagtcc ccgcattcca gtgcatggaa cccttctggc
                                                                       480
ctccctgtat aagtccagac tgaaaccccc ttggaaggnc tccagtcagg cagccctana
                                                                       540
aactggggaa aaaagaaaag gacgcccan cccccagctg tgcanctacg cacctcaaca
                                                                       600
qcacagggtg qcagcaaaaa aaccacttta ctttggcaca aacaaaaact nqqqqqqa
                                                                       660
acceeggeac ecenangggg gttaacagga anengggnaa entggaacce aattnaggea
                                                                       720
ggcccnccac cccnaatntt gctgggaaat ttttcctccc ctaaattntt tc
      <210> 12
      <211> 751
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(751)
      \langle 223 \rangle n = A,T,C or G
      <400> 12
gccccaattc cagctgccac accacccacg gtgactgcat tagttcggat gtcatacaaa
                                                                        60
agctgattga agcaaccctc tactttttgg tcgtgagcct tttgcttggt gcaggtttca
                                                                       120
ttggctgtgt tggtgacgtt gtcattgcaa cagaatgggg gaaaggcact gttctctttg
                                                                       180
aaqtanggtg agtcctcaaa atccgtatag ttggtgaagc cacagcactt gagccctttc
                                                                       240
atggtggtgt tecacacttg agtgaagtet teetgggaac cataatettt ettgatggca
                                                                       300
ggcactacca gcaacgtcag ggaagtgctc agccattgtg gtgtacacca aggcgaccac
                                                                       360
agcagetgen aceteageaa tgaagatgan gaggangatg aagaagaacg tenegaggge
                                                                       420
acacttgctc tcagtcttan caccatanca gcccntgaaa accaananca aagaccacna
                                                                       480
cnccggctgc gatgaagaaa tnaccccncg ttgacaaact tgcatggcac tggganccac
                                                                       540
agtggcccna aaaatcttca aaaaggatgc cccatcnatt gaccccccaa atgcccactg
                                                                       600
ccaacagggg ctgccccacn cncnnaacga tganccnatt gnacaagatc tncntggtct
                                                                       660
tnatnaacht gaaccetgen tngtggetee tgtteaggne ennggeetga ettetnaann
                                                                       720
aangaacten gaagneecca enggananne g
                                                                       751
      <210> 13
      <211> 729
```

```
<220>
       <221> misc_feature
       <222> (1)...(729)
       \langle 223 \rangle n = A,T,C or G
       <400> 13
 gagecaggeg tecetetgee tgeceaetea gtggeaacae eegggagetg ttttgteett
                                                                         60
 tgtggancct cagcagtncc ctctttcaga actcantgcc aaganccctg aacaggagcc
                                                                        120
accatgcagt gcttcagctt cattaagacc atgatgatcc tcttcaattt gctcatcttt
                                                                        180
 ctgtgtggtg cagccctgtt ggcagtgggc atctgggtgt caatcgatgg ggcatccttt
                                                                        240
ctgaagatct tcgggccact gtcgtccagt gccatgcagt ttgtcaacgt gggctacttc
                                                                        300
ctcatcgcag ccggcgttgt ggtcttagct ctaggtttcc tgggctgcta tggtgctaag
                                                                        360
actgagagca agtgtgccct cgtgacgttc ttcttcatcc tcctcctcat cttcattgct
                                                                        420
gaggttgcaa tgctgtggtc gccttggtgt acaccacaat ggctgagcac ttcctgacgt
                                                                        480
tgctggtaat gcctgccatc aanaaaagat tatgggttcc caggaanact tcactcaagt
                                                                        540
gttggaacac caccatgaaa gggctcaagt gctgtggctt cnnccaacta tacggatttt
                                                                        600
gaagantcac ctacttcaaa gaaaanagtg cctttccccc atttctgttg caattgacaa
                                                                        660
acgtececaa cacagecaat tgaaaacetg cacecaacee aaangggtee ccaaccanaa
                                                                        720
attnaaggg
                                                                        729
      <210> 14
      <211> 816
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(816)
      <223> n = A,T,C or G
      <400> 14
tgctcttcct caaagttgtt cttgttgcca taacaaccac cataggtaaa gcgggcgcag
tgttcgctga aggggttgta gtaccagcgc gggatgctct ccttgcagag tcctgtgtct
                                                                       120
ggcaggtcca cgcagtgccc tttgtcactg gggaaatgga tgcgctggag ctcgtcaaag
                                                                       180
ccactegtgt attiticaca ggeagecteg teegaegegt eggggeagtt gggggtgtet
                                                                       240
tcacacteca ggaaactgte natgeageag ceattgetge ageggaactg ggtgggetga
                                                                       300
cangigecag ageacactgg atggegeett tecatgnnan gggeeetgng ggaaagteee
                                                                       360
tganccccan anctgectet caaangeeee acettgeaca eeeegacagg etagaatgga
                                                                       420
atcttcttcc cgaaaggtag ttnttcttgt tgcccaancc anccccntaa acaaactctt
                                                                       480
gcanatctgc teegnggggg tentantacc ancgtgggaa aagaacccca ggengegaac
                                                                       540
caancttgtt tggatncgaa gcnataatct nctnttctgc ttggtggaca gcaccantna
                                                                       600
ctgtnnanct ttagncentg gtcctcntgg gttgnncttg aacctaatcn ccnntcaact
                                                                       660
gggacaaggt aantngcent cetttnaatt ecenanentn eeeetggtt tggggttttn
                                                                       720
cnenetecta ecceagaaan neegtgttee ecceeaacta ggggeenaaa cenntintte
                                                                       780
cacaaccctn ccccacccac gggttcngnt ggttng
                                                                       816
      <210> 15
      <211> 783
      <212> DNA
      <213> Homo sapien
      <220>
```

<221> misc\_feature
<222> (1)...(783)
<223> n = A,T,C or G

```
<400> 15
ccaaggcctg ggcaggcata nacttgaagg tacaacccca ggaacccctg gtgctgaagg
                                                                        60
atgtggaaaa cacagattgg cgcctactgc ggggtgacac ggatgtcagg gtagagagga
                                                                       120
aagacccaaa ccaggtggaa ctgtggggac tcaaggaang cacctacctg ttccagctga
                                                                       180
cagtgactag ctcagaccac ccagaggaca cggccaacgt cacagtcact gtgctqtcca
                                                                       240
ccaagcagac agaagactac tgcctcgcat ccaacaangt gggtcgctgc cgggggctctt
                                                                       300
teceaegetg gtactatgae eccaeggage agatetgeaa gagtttegtt tatggagget
gcttgggcaa caagaacaac taccttcggg aagaagagtg cattctancc tgtcngggtg
                                                                       420
tgcaaggtgg gcctttgana ngcanctctg gggctcangc gactttcccc cagggcccct
                                                                       480
ccatggaaag gcgccatcca ntgttctctg gcacctgtca gcccacccag ttccgctgca
                                                                       540
ncaatggctg ctgcatcnac antitcctng aattgtgaca acacccccca ntgcccccaa
                                                                       600
ccctcccaac aaagcttccc tgttnaaaaa tacnccantt ggcttttnac aaacncccgg
                                                                       660
cncctccntt ttccccnntn aacaaagggc nctngcnttt gaactgcccn aacccnggaa
                                                                       720
tetneenngg aaaaantnee eeceetggtt eetnnaance eeteenenaa anetneecee
                                                                       780
                                                                       783
      <210> 16
      <211> 801
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(801)
      <223> n = A,T,C or G
      <400> 16
gccccaattc cagctgccac accacccacg gtgactgcat tagttcggat gtcatacaaa
                                                                        60
agctgattga agcaaccete tactttttgg tegtgageet tttgettggt geaggtttea
                                                                      120
ttggctgtgt tggtgacgtt gtcattgcaa cagaatgggg gaaaggcact gttctctttg
                                                                       180
aagtagggtg agtcotcaaa atcogtatag ttggtgaagc cacagcactt gagcoctttc
                                                                      240
atggtggtgt tccacacttg agtgaagtct tcctgggaac cataatcttt cttgatggca
                                                                      300
ggcactacca gcaacgtcag gaagtgctca gccattgtgg tgtacaccaa ggcgaccaca
                                                                      360 ·
gcagctgcaa cctcagcaat gaagatgagg aggaggatga agaagaacgt cncgagggca
                                                                      420
cacttgctct ccgtcttagc accatagcag cccangaaac caagagcaaa gaccacaacg
                                                                      480
congotgoga atgaaagaaa ntacccaogt tgacaaactg catggccact ggacgacagt
                                                                      540
tggcccgaan atcttcagaa aagggatgcc ccatcgattg aacacccana tgcccactgc
                                                                      600
cnacaggget geneenenen gaaagaatga gecattgaag aaggatente ntggtettaa
                                                                      660
tgaactgaaa ccntgcatgg tggcccctgt tcagggctct tggcagtgaa ttctganaaa
                                                                      720
aaggaacngc ntnagccccc ccaaangana aaacaccccc gggtgttgcc ctgaattggc
                                                                      780
ggccaaggan ccctgccccn g
                                                                      801
      <210> 17
      <211> 740
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(740)
      <223> n = A,T,C or G
```

<400> 17

```
cctttgtgga gcctcagcag ttccctcttt cagaactcac tgccaagagc cctgaacagg
                                                                          120
 agccaccatg cagtgettea getteattaa gaccatgatg atcetettea atttgeteat
                                                                          180
 ctttctgtgt ggtgcagccc tgttggcagt gggcatctgg gtgtcaatcg atggggcatc
                                                                         240
 ctttctgaag atcttcgggc cactgtcgtc cagtgccatg cagtttgtca acgtgggcta
                                                                         300 _
 cttcctcatc gcagccggcg ttgtggtctt tgctcttggt ttcctgggct gctatggtgc
                                                                         360
 taagacggag agcaagtgtg ccctcgtgac gttcttcttc atcctcctcc tcatcttcat
                                                                         420
 tgctgaagtt gcagctgctg tggtcgcctt ggtgtacacc acaatggctg aaccattcct
                                                                         480 -
 gacgttgctg gtantgcctg ccatcaanaa agattatggg ttcccaggaa aaattcactc
                                                                         540
 aantntggaa caccnccatg aaaagggctc caatttctgn tggcttcccc aactataccg
                                                                         600
 gaattttgaa aganteneec taetteeaaa aaaaaanant tgeetttnee eeenttetgt
                                                                         660
 tgcaatgaaa acntcccaan acngccaatn aaaacctgcc cnnncaaaaa ggntcncaaa
                                                                         720
 caaaaaant nnaagggttn
                                                                         740
       <210> 18
       <211> 802
       <212> DNA
       <213> Homo sapien
       <220>
       <221> misc_feature
       <222> (1)...(802)
       \langle 223 \rangle n = A,T,C or G
       <400> 18
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                                                                         60
 caaggtette cagetgeege acattaegea gggcaagage etecageaac actgeatatg
                                                                        120
ggatacactt tactttagca gccagggtga caactgagag gtgtcgaagc ttattcttet
                                                                        180
gagectetgt tagtggagga agatteeggg etteagetaa gtagteageg tatgteecat
                                                                        240
aagcaaacac tgtgagcagc cggaaggtag aggcaaagtc actctcagcc agctctctaa
                                                                        300
cattgggcat gtccagcagt tctccaaaca cgtagacacc agnggcctcc agcacctgat
                                                                        360
ggatgagtgt ggccagcgct gcccccttgg ccgacttggc taggagcaga aattgctcct
                                                                        420
ggttctgccc tgtcaccttc acttccgcac tcatcactgc actgagtgtg ggggacttgg
                                                                        480
getcaggatg tecagagaeg tggtteegee eeetenetta atgacaeegn ceanneaace
                                                                        540
gtcggctccc gccgantgng ttcgtcgtnc ctgggtcagg gtctgctggc cnctacttgc
                                                                        600
aancttcgtc nggcccatgg aattcaccnc accggaactn gtangatcca ctnnttctat
                                                                        660
aaccggncgc caccgcnnnt ggaactccac tetintinec titacitgag ggttaaggte
                                                                        720
accettnneg ttacettggt ccaaacentn centgtgteg anatngtnaa tenggneena
                                                                        780.
tnccancene atangaagee ng
                                                                        802
      <210> 19
      <211> 731
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(731)
      \langle 223 \rangle n = A,T,C or G.
      <400> 19
cnaagettee aggtnaeggg eegenaanee tgaeeenagg tancanaang eagnengegg
                                                                         60
gagcccaccg tcacgnggng gngtctttat nggaggggc ggagccacat cnctggacnt
                                                                        120
entgacecca acteccence nencantgea gtgatgagtg cagaactgaa ggtnacgtgg
                                                                        180
caggaaccaa gancaaanne tgeteennte caagteggen nagggggegg ggetggecae
                                                                        240
geneateent enagtgetgn aaageeeenn eetgtetaet tgtttggaga aengennnga
                                                                       300
```

```
catgcccagn gttanataac nggcngagag tnantttgcc tctcccttcc ggctgcgcan
                                                                        360
 cgngtntgct tagnggacat aacctgacta cttaactgaa cccnngaatc tnccnccct
                                                                        420
ccactaagct cagaacaaaa aacttcgaca ccactcantt gtcacctgnc tgctcaagta
                                                                        480
aagtgtaccc catneccaat gtntgetnga ngetetgnee tgenttangt teggteetgg
                                                                        540
gaagacctat caattnaagc tatgtttctg actgcctctt gctccctgna acaancnacc
                                                                        600
cnncnntcca aggggggnc ggcccccaat ccccccaacc ntnaattnan tttancccn
                                                                        660
cccccnggcc cggcctttta cnancntcnn nnacngggna aaaccnnngc tttncccaac
                                                                       -720
nnaatccncc t
                                                                        731
      <210> 20
      <211> 754
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(754)
      \langle 223 \rangle n = A,T,C or G
      <400> 20
ttttttttt tttttttt taaaaacccc ctccattnaa tgnaaacttc cgaaattgtc
                                                                        60
caaccccctc ntccaaatnn contttccgg gngggggttc caaacccaan ttanntttgg
                                                                       120
annttaaatt aaatnttnnt tggnggnnna anccnaatgt nangaaagtt naacccanta
                                                                       180
tnancttnaa tncctggaaa congtngntt ccaaaaatnt ttaaccctta antccctccg
                                                                       240
aaatngttna nggaaaaccc aanttctcnt aaggttgttt gaaggntnaa tnaaaanccc
                                                                       300
nnccaattgt ttttngccac gcctgaatta attggnttcc gntgttttcc nttaaaanaa
                                                                       360
ggnnancccc ggttantnaa tccccccnnc cccaattata ccganttttt ttngaattgg
                                                                       420
gancecnegg gaattaacgg ggnnnntece tnttgggggg enggnnece eccenteggg
                                                                       480
ggttngggnc aggncnnaat tgtttaaggg tccgaaaaat ccctccnaga aaaaaanctc
                                                                       540
ccaggntgag nntngggttt ncccccccc canggcccct ctcgnanagt tggggtttgg
                                                                       600
ggggcctggg attttntttc ccctnttncc tcccccccc ccnggganag aggttngngt
                                                                       660
tttgntcnnc ggccccnccn aaganctttn ccganttnan ttaaatccnt gcctnggcga
                                                                       720
agtccnttgn agggntaaan ggccccctnn cggg
                                                                       754
      <210> 21
      <211> 755
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(755)
      <223> n = A,T,C or G
      <400> 21
atcancccat gaccccnaac nngggaccnc tcanccggnc nnncnaccnc cggccnatca
                                                                        60
nngtnagnne actnennttn nateaeneee eneenaetae geeenenane enaegeneta
                                                                       120
nncanatnee actganngeg egangtngan ngagaaanet nataccanag neaccanaen
                                                                       180
ccagctgtcc nanaangcct nnnatacngg nnnatccaat ntgnancctc cnaagtattn
                                                                       240
nncnncanat gattttcctn anccgattac centnecece tanecectec ecceaacna
                                                                       300
egaaggenet ggneenaagg nngegnenee eegetagnte eeenneaagt eneneneeta
                                                                       360
aactcancen nattaenege ttentgagta teacteeceg aateteacee tactcaacte
                                                                       420
aaaaanatcn gatacaaaat aatncaagcc tgnttatnac actntgactg ggtctctatt
                                                                       480
ttagnggtcc ntnaancntc ctaatacttc cagtctncct tcnccaattt ccnaanggct
                                                                       540
ctttcngaca gcatnttttg gttcccnntt gggttcttan ngaattgccc ttcntngaac
```

gggctcntct tttccttcgg ttancctggn ttcnnccggc cagttattat ttcccntttt

```
aaattentne entttanttt tggenttena aaceceegge ettgaaaaeg geeecetggt
                                                                         720
 aaaaggttgt tttganaaaa tttttgtttt gttcc
                                                                         755
       <210> 22
       <211> 849
       <212> DNA
       <213> Homo sapien
       <220>
       <221> misc_feature
       <222> (1) ... (849)
       \langle 223 \rangle n = A,T,C or G
       <400> 22
ttttttttt tttttangtg tngtcgtgca ggtagaggct tactacaant gtgaanacgt
                                                                         60
acgcinggan taangcgacc cgantictag gannencect aaaatcanac tgigaagain
                                                                        120
atcctgnnna cggaanggtc accggnngat nntgctaggg tgnccnctcc cannnenttn
                                                                        180
cataacteng nggccctgcc caccaccttc ggcggcccng ngnccgggcc cgggtcattn
                                                                        240
gnnttaacen caetnngena neggttteen neecenneng accenggega teeggggtne
                                                                        300.
tetgtettee cetgnagnen anaaantggg ceneggneee etttaceeet nnacaageea
                                                                        360
engeenteta neenengeee eeeeteeant nngggggaet geenannget eegttnetng
                                                                        420
nnaccconnn gggtncctcg gttgtcgant chaccgnang ccanggattc cnaaggaagg
                                                                        480
tgcgttnttg gcccctaccc ttcgctncgg nncacccttc ccgacnanga nccgctcccg
                                                                        540
enennegning cetenecteg caacacege netentengt neggninece ecceacege
                                                                        600
necetenene ngnegnanen eteeneenee gteteannea eeaceegee eegeeaggee
                                                                        660
ntcanccach ggnngachng nagchennte geneegegen gegneneet egeenengaa
                                                                        720
ctnentengg ccantingec teaaneenna enaaacgeeg etgegeggee egnagegnee
                                                                        780
necteenega gteeteeegn etteenacee anguntteen egaggaeaen unaceeegee
                                                                        840
nncangcgg
                                                                        849
      <210> 23
      <211> 872
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(872)
      \langle 223 \rangle n = A,T,C or G
      <400> 23
gcgcaaacta tacttcgctc gnactcgtgc gcctcgctnc tctttcctc cgcaaccatg
                                                                        60
tctgacnanc ccgattnggc ngatatcnan aagntcganc agtccaaact gantaacaca
                                                                        120
cacacnonan aganaaatco notgoottoo anagtanaon attgaacnng agaaccango
                                                                       180
nggcgaatcg taatnaggcg tgcgccgcca atntgtcncc gtttattntn ccagcntcnc
                                                                       240
etnecnacce tachtetten nagetgtenn acceetngth egnaceeece naggteggga
                                                                       300
tegggtttnn nntgacegng enneceetee eccenteeat nacganeene eegeaceaee
                                                                       360
nanngenege neecegnnet ettegeenee etgteetntn eccetgtnge etggenengn
                                                                       420
accgcattga ccctcgccnn ctncnngaaa ncgnanacgt ccgggttgnn annancgctg
                                                                       480
tgggnnngcg tetgencege gtteetteen nennetteea ceatettent taengggtet
                                                                       540
conegeonte tennneache eetgggaege thteethtge ecceetthae tecceecett
                                                                       600
egnegtgnee egneeceace nteatttnea naegntette acaannneet ggntnnetee
                                                                       660
cnancngncn gtcancenag ggaagggngg ggnneenntg nttgacgttg nggngangte
                                                                       720
cgaanantcc tencentean enctaceeet egggegnnet etengttnee aaettaneaa
                                                                       780
```

```
ntctcccccg ngngcncntc tcagcctcnc ccnccccnct ctctgcantg tnctctgctc
                                                                        840
tnaccnntac gantnttcgn cnccctcttt cc
                                                                        872
      <210> 24
      <211> 815
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1) ... (815)
      \langle 223 \rangle n = A,T,C or G
      <400> 24
gcatgcaagc ttgagtattc tatagngtca cctaaatanc ttggcntaat catggtcnta
                                                                        60
nctgncttcc tgtgtcaaat gtatacnaan tanatatgaa tctnatntga caaganngta
                                                                       120
tentneatta gtaacaantg tnntgteeat eetgtengan canatteeca tnnattnegn
                                                                       180
cgcattcncn gcncantatn taatngggaa ntcnnntnnn ncaccnncat ctatcntncc
                                                                       240
geneeetgae tggnagagat ggatnantte tnntntgace nacatgttea tettggattn
                                                                       300
aanancecee egengneeae eggtingning enageennite ecaagacete etgiggaggt
                                                                       360
aacctgcgtc aganncatca aacntgggaa acccgcnncc angtnnaagt ngnnncanan
                                                                       420
gatecegtee aggnttnace atceettene agegeeecet tingtgeett anagngnage
                                                                       480
gtgtccnanc cnctcaacat ganacgcgcc agnccanccg caattnggca caatgtcgnc
                                                                       540
gaacccccta gggggantna tncaaanccc caggattgtc cncncangaa atcccncanc
                                                                       600
cccnccctac ccnnctttgg gacngtgacc aantcccgga gtnccagtcc ggccngnctc
                                                                       660
ccccaccggt nnccntgggg gggtgaanct cngnntcanc cngncgaggn ntcgnaagga
                                                                       720
accggncctn ggncgaanng ancnntcnga agngccncnt cgtataaccc cccctcncca
ncenacignt agricecce enggginegg aangg
      <210> 25
      <211> 775
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc feature
      <222> (1)...(775)
      <223> n = A,T,C or G
      <400> 25
ccgagatgtc tcgctccgtg gccttagctg tgctcgcgct actctctctt.tctggcctgg
aggetateca gegtaeteca aagatteagg tttaeteacg teatecagea gagaatggaa
                                                                       120
agtcaaattt cctgaattgc tatgtgtctg ggtttcatcc atccgacatt gaanttgact
                                                                       180
tactgaagaa tgganagaga attgaaaaag tggagcattc agacttgtct ttcagcaagg
                                                                       240
actggtcttt ctatctcntg tactacactg aattcacccc cactgaaaaa gatgagtatg
                                                                       300
cctgccgtgt gaaccatgtg actttgtcac agcccaagat agttaagtgg gatcgagaca
                                                                       360
tgtaagcagn cnncatggaa gtttgaagat gccgcatttg gattggatga attccaaatt
ctgcttgctt gcnttttaat antgatatgc ntatacaccc taccctttat gnccccaaat
                                                                       480
tgtaggggtt acatnantgt tenentngga catgatette etttataant cencentteg
                                                                       540
aattgcccgt cncccngttn ngaatgtttc cnnaaccacg gttggctccc ccaggtcncc
                                                                       600
tettaeggaa gggeetggge enetttneaa ggttggggga acenaaaatt tenettntge
                                                                       660
conceencea enntettgng nneneanttt ggaaccette enatteecet tggeetenna
                                                                       720
nccttnncta anaaaacttn aaancgtngc naaanntttn acttccccc ttacc
                                                                       775
```

```
<211> 820
       <212> DNA
       <213> Homo sapien
       <220>
       <221> misc_feature
       <222> (1)...(820)
       <223> n = A,T,C or G
       <400> 26
 anattantac agtgtaatct tttcccagag gtgtgtanag ggaacggggc ctagaggcat
                                                                         60
 cccanagata nettatanea acagtgettt gaccaagage tgetgggeae attteetgea
                                                                        120
 gaaaaggtgg cggtccccat cactcctcct ctcccatagc catcccagag gggtgagtag
                                                                        180
ccatcangcc ttcggtggga gggagtcang gaaacaacan accacagagc anacagacca
                                                                        240
 ntgatgacca tgggcgggag cgagcctctt ccctgnaccg gggtggcana nganagccta
                                                                        300
 nctgaggggt cacactataa acgttaacga ccnagatnan cacctgcttc aagtgcaccc
                                                                        360
 ttcctacctg acnaccagng accnnnaact gcngcctggg gacagcnctg ggancagcta
                                                                        420
acnnageact cacetgeece eccatggeeg thegenteec tggteetgne aagggaaget
                                                                        480
ccctgttgga attncgggga naccaaggga nccccctcct ccanctgtga aggaaaaann
                                                                        540
gatggaattt thecetteeg geennteece tetteettta caegeeceet nntactente
teeetetntt nteetgnene aettttnace eennnattte eettnattga teggannetn
                                                                       660
ganattecae tnnegeetne entenateng naanacnaaa naetntetna eeenggggat
                                                                       720
gggnncctcg ntcatcctct ctttttcnct accnccnntt ctttgcctct ccttngatca
780tccaacente gntggeentn ecceeennn teetttneee
      <210> 27
      <211> 818
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(818)
      <223> n = A,T,C or G
      <400> 27
totgggtgat ggcctcttcc toctcaggga cotctgactg ctctgggcca aagaatotot
tgtttcttct ccgagcccca ggcagcggtg attcagccct gcccaacctg attctgatga
                                                                       120
ctgcggatgc tgtgacggac ccaaggggca aatagggtcc cagggtccag ggaggggcgc
                                                                       180
ctgctgagca cttccgcccc tcaccctgcc cagcccctgc catgagctct gggctgggtc
                                                                       240
teegeeteea gggttetget etteeangea ngeeancaag tggegetggg ceacactgge
                                                                       300
ttetteetge ecentecetg getetgante tetgtettee tgteetgtge angeneettg
                                                                       360
gateteagtt teectenete anngaactet gtttetgann tetteantta actntgantt
                                                                       420
tatnaccnan tggnctgtnc tgtcnnactt taatgggccn gaccggctaa tccctcctc
                                                                       480
netecettee anttennnna accngettne ententetee centaneceg cengggaane
                                                                       540
ctcctttgcc ctnaccangg gccnnnaccg cccntnnctn ggggggcnng gtnnctncnc
                                                                       600
ctgntnnccc enctenennt thectegtee ennennegen nngeanntte nengteeenn
                                                                       660
tnnctcttcn ngtntcgnaa ngntcncntn tnnnnngncn ngntnntncn tccctctcnc
                                                                       720
ennntgnang tnnttnnnne nengnneece nnnnennnnn nggnnntnnn tetnenenge
                                                                       780
cccnncccc ngnattaagg cctccnntct ccggccnc
                                                                       818
      <210> 28
      <211> 731
```

<212> DNA

<221> misc\_feature

```
<213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(731)
      \langle 223 \rangle n = A,T,C or G
      <400> 28
aggaagggcg gagggatatt gtangggatt gagggatagg agnataangg gggaggtgtg
                                                                         60
teceaacatg anggtgnngt tetettttga angagggttg ngtttttann cenggtgggt
                                                                        120
gattnaaccc cattgtatgg agnnaaaggn tttnagggat ttttcggctc ttatcagtat
                                                                        180
ntanatteet gtnaategga aaatnatntt tennenggaa aatnttgete eeateegnaa
                                                                        240
attnetcecg ggtagtgcat nttngggggn engecangtt teccaggetg ctanaategt
                                                                        300
actaaagntt naagtgggan tncaaatgaa aacctnncac agagnatcon tacccgactg
                                                                        360
trinitinect tegeeethig actetgening ageceaatac connignment grenecomm
                                                                        420
nnngegnene tgaaannnne tegnggetnn gancateang gggtttegea teaaaagenn
                                                                        480
egttteneat naaggeactt tngceteate caacenetng eeetenneea tttngeegte
                                                                        540
nggttenect aegetnntng encetnnntn ganattttne cegeetnggg naanceteet
                                                                        600
gnaatgggta gggnettnte tittnacenn gnggintaet aatenneine acgeninett
                                                                        660
tetenacece ceceetttt caateeeane ggenaatggg gteteeeenn eganggggg
                                                                        720
nnncccannc c
                                                                        731
      <210> 29
      <211> 822
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(822)
      \langle 223 \rangle n = A,T,C or G
      <400> 29
actagtecag tgtggtggaa ttecattgtg ttggggnene ttetatgant anthttagat
                                                                         60
cgctcanacc tcacancctc ccnacnangc ctataangaa nannaataga nctgtncnnt
                                                                        120
aththtache teatanneet ennnaceeae teeetettaa eeentaetgt geetatngen
                                                                        180
tnnctantct ntgccgcctn cnanccaccn gtgggccnac cncnngnatt ctcnatctcc
                                                                        240
tenecatntn geetananta ngtneatace etatacetae necaatgeta nnnetaanen
                                                                        300
tocatnantt annntaacta coactgacht ngactttene athanetect aatttgaate
                                                                        360
tactctgact cccacngcct annnattagc anchtececc nacnathtet caaccaaate
                                                                        420
ntcaacaacc tatctanctg ttcnccaacc nttncctccg atccccnnac aaccccctc
                                                                        480
ccaaataccc nccacctgac ncctaacccn caccatcccg gcaagccnan ggncatttan
                                                                        540
ccactggaat cacnatngga naaaaaaaac ccnaactctc tancncnnat ctccctaana
                                                                        600
aatneteetn naatttaetn neantneeat caaneeeaen tgaaaennaa eeeetgtttt
                                                                        660
tanatecett etttegaaaa eenaeeettt annneeeaac etttngggee eeceenetne
                                                                        720
ccnaatgaag gncncccaat cnangaaacg nccntgaaaa ancnaggcna anannntccg
                                                                        780
canatectat ecettantin ggggneeett neeengggee ee
                                                                        822
      <210> 30
      <211> 787
      <212> DNA
      <213> Homo sapien
      <220>
```

```
<222> (1)...(787)
<223> n = A,T,C or G
```

<400> 30 cggccgcctg ctctggcaca tgcctcctga atggcatcaa aagtgatgga ctgcccattg 60 ctagagaaga ccttctctcc tactgtcatt atggagccct gcagactgag ggctcccctt 120 gtctgcagga tttgatgtct gaagtcgtgg agtgtggctt ggagctcctc atctacatna 180 gctggaagcc ctggagggcc tctctcgcca gcctccccct tctctccacg ctctccangg 240 acaccagggg ctccaggcag cccattattc ccagnangac atggtgtttc tccacgcgga 300 cccatggggc ctgnaaggcc agggtctcct ttgacaccat ctctcccgtc ctgcctggca 360 ggccgtggga tccactantt ctanaacggn cgccaccncg gtgggagctc cagcttttgt 420 tecenttaat gaaggttaat tgenegettg gegtaateat nggteanaac tnttteetgt 480 gtgaaattgt ttntcccctc ncnattccnc ncnacatacn aacceggaan cataaagtgt 540 taaagcctgg gggtngcctn nngaatnaac tnaactcaat taattgcgtt ggctcatggc 600 ccgctttccn ttcnggaaaa ctgtcntccc ctgcnttnnt gaatcggcca cccccnggg 660 aaaagcggtt tgcnttttng ggggntcctt concttecce cetenetaan ceetnegeet 720 eggtegttne nggtngeggg gaangggnat nnnetecene naagggggng agnnngntat 780 ccccaaa 787

<210> 31

<211> 799

<212> DNA

<213> Homo sapien

<220>

<221> misc\_feature

<222> (1) . . . (799)

<223> n = A,T,C or G

## <400> 31

ttttttttt tttttttggc gatgctactg tttaattgca ggaggtgggg gtgtgtgtac catgtaccag ggctattaga agcaagaagg aaggagggag ggcagagcgc cctgctgagc 120 aacaaaggac teetgeagee ttetetgtet gtetettgge geaggeacat ggggaggeet 180 cccgcagggt gggggccacc agtccagggg tgggagcact acanggggtg ggagtgggtg 240 gtggctggtn cnaatggcct gncacanatc cctacgattc ttgacacctg gatttcacca 300 ggggacette tgttetecca nggnaactte ntnnateten aaagaacaca actgtttett 360 . engeanttet ggetgtteat ggaaageaca ggtgteenat ttnggetggg acttggtaca 420. tatggttccg gcccacctct cccntcnaan aagtaattca ccccccccn centctnttg 480 cctgggccct taantaccca caccggaact canttantta ttcatcttng gntgggcttg 540 ntnateneen cetgaangeg ceaagttgaa aggeeaegee gtnecenete eecatagnan 600 . nttttnncnt canctaatgc ccccccnggc aacnatccaa teccecccn tgggggcccc 660 ageceangge eccegneteg ggnnneengn enegnantee ecaggntete ceantengne 720 conningence ecceptacea gaacanaagg ntngageene egeanninni nggtinenae 780 ctcgccccc ccnncgnng 799

<210> 32

<211> 789

<212> DNA

<213> Homo sapien

<220>

<221> misc\_feature

<222> (1) ... (789)

<223> n = A,T,C or G

```
<400> 32
60
ttttnccnag ggcaggttta ttgacaacct cncgggacac aancaggctg gggacaggac
                                                                     120
ggcaacaggc tccggcggcg gcggcggcgg ccctacctgc ggtaccaaat ntgcagcctc
                                                                     180
egeteeeget tgatntteet etgeagetge aggatgeent aaaacaggge eteggeentn
                                                                     240
ggtgggcacc ctgggatttn aatttccacg ggcacaatgc ggtcgcancc cctcaccacc
                                                                     300
nattaggaat agtggtntta cccnccnccg ttggcncact ccccntggaa accacttntc
                                                                    360
geggeteegg catetggtet taaacettge aaacnetggg gecetetttt tggttantnt
                                                                     420
nccngccaca atcatnactc agactggcnc gggctggccc caaaaaancn ccccaaaacc
                                                                     480
ggnccatgtc ttnncggggt tgctgcnatn tncatcacct cccgggcnca ncaggncaac
                                                                     540
ccaaaagttc ttgnggcccn caaaaaanct ccggggggnc ccagtttcaa caaagtcatc
                                                                     600
ccccttggcc cccaaatcct ccccccgntt nctgggtttg ggaacccacg cctctnnctt
                                                                     660
tggnnggcaa gntggntccc ccttcgggcc cccggtgggc ccnnctctaa ngaaaacncc
                                                                     720
ntectnnnea ceateceece nngnnaegne tancaangna teeettttt tanaaaeggg
                                                                     780
cccccncg
                                                                     789
      <210> 33
      <211> 793
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(793)
      <223> n = A,T,C or G
      <400> 33
gacagaacat gttggatggt ggagcacctt tctatacgac ttacaggaca gcagatgggg
                                                                     60
aattcatggc tgttggagca atanaacccc agttctacga gctgctgatc aaaggacttg
                                                                     120
gactaaagtc tgatgaactt cccaatcaga tgagcatgga tgattggcca gaaatgaana
agaagtttgc agatgtattt gcaaagaaga cgaaggcaga gtggtgtcaa atctttgacg
                                                                    240
gcacagatgc ctgtgtgact ccggttctga cttttgagga ggttgttcat catgatcaca
                                                                    300
acaangaacg gggctcgttt atcaccantg aggagcagga cgtgagcccc cgccctgcac
                                                                    360
ctctgctgtt aaacacccca gccatccctt ctttcaaaag ggatccacta cttctagagc
                                                                    420
ggncgccacc gcggtggagc tccagctttt gttcccttta gtgagggtta attgcgcgct
                                                                    480
tggcgtaatc atggtcatan ctgtttcctg tgtgaaattg ttatccgctc acaattccac
                                                                    540
acaacatacg anceggaage atnaaatttt aaageetggn ggtngeetaa tgantgaact
                                                                    600
nactcacatt aattggcttt gegeteactg ceegetttee agteeggaaa acetgteett
                                                                    660
gccagctgcc nttaatgaat cnggccaccc cccggggaaa aggcngtttg cttnttgggg
                                                                    720
cgcncttccc gctttctcgc ttcctgaant ccttcccccc ggtctttcgg cttgcggcna
                                                                    780
acggtatcna cct
                                                                    793
      <210> 34
      <211> 756
      <212> DNA
     <213> Homo sapien
      <220>
     <221> misc feature
     <222> (1)...(756)
     <223> n = A,T,C or G
     <400> 34
gccgcgaccg gcatgtacga gcaactcaag ggcgagtgga accgtaaaag ccccaatctt
                                                                     60
ancaagtgcg gggaanagct gggtcgactc aagctagttc ttctggagct caacttcttg
                                                                    120
```

```
ccaaccacag ggaccaagct gaccaaacag cagctaattc tggcccgtga catactggag
                                                                        180
 ateggggeec aatggageat cetaegeaan gacateceet cettegageg ctacatggee
                                                                        240
 cageteaaat getaetaett tgattacaan gageagetee eegagteage etatatgeae
                                                                        300
 cagetettgg geeteaacet cetetteetg etgteecaga acegggtgge tgantnecae
                                                                        360
 acgganttgg ancggctgcc tgcccaanga catacanacc aatgtctaca tcnaccacca
                                                                        420
 gtgtcctgga gcaatactga tgganggcag ctaccncaaa gtnttcctgg ccnagggtaa
                                                                        480
catececege egagagetae acettettea ttgacatect getegacaet atcagggatg
                                                                        540
aaaatcgcng ggttgctcca gaaaggctnc aanaanatcc ttttcnctga aggccccgg
                                                                        600
atnonctagt notagaatcg geoegecatc geggtgganc ctccaacctt tegttnecct
                                                                        660
ttactgaggg ttnattgccg cccttggcgt tatcatggtc acnccngttn cctgtgttga
                                                                        720
aattnttaac cccccacaat tccacgccna cattng
                                                                        756
      <210> 35
      <211> 834
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1) ... (834)
      <223> n = A,T,C or G
      <400> 35
ggggatctct anatchacct gnatgcatgg ttgtcggtgt ggtcgctgtc gatgaanatg
                                                                         60
aacaggatet tgeeettgaa getetegget getgtnttta agttgeteag tetgeegtea
                                                                       120
tagtcagaca cnctcttggg caaaaaacan caggatntga gtcttgattt cacctccaat
                                                                       180
aatcttengg getgtetget eggtgaacte gatgaenang ggeagetggt tgtgtntgat
                                                                       240
aaantccanc angtteteet tggtgacete eeetteaaag ttgtteegge etteateaaa
                                                                       300
cttctnnaan angannance canctttgte gagetggnat ttgganaaca egtcactgtt
                                                                       360
ggaaactgat cccaaatggt atgtcatcca tcgcctctgc tgcctgcaaa aaacttgctt
                                                                       420
ggcncaaatc cgacteccen teettgaaag aageenatea cacececte cetggactee
                                                                       480
nncaangact ctnccgctnc cccntccnng cagggttggt ggcannccgg gcccntgcgc
                                                                       540
ttetteagee agtteaenat ntteateage ecetetgeea getgttntat teettggggg
                                                                       600
ggaancegte tetecettee tgaannaact ttgacegtng gaatageege genteneent
                                                                       660
achthology coggetteaa anteceteen tighennien celegggeea tietggatti
                                                                       720
nccnaacttt ttccttcccc cnccccncgg ngtttggntt tttcatnggg ccccaactct
                                                                       780
getnttggee anteceetgg gggentntan eneceeetnt ggteeentng ggee
                                                                       834
      <210> 36
      <211> 814
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature .
      <222> (1)...(814)
      \langle 223 \rangle n = A,T,C or G
     . <400> 36
cggncgcttt ccngccgcgc cccgtttcca tgacnaaggc tcccttcang ttaaatacnn
                                                                        60
cctagnaaac attaatgggt tgctctacta atacatcata cnaaccagta agcctgccca
                                                                       120
naacgccaac tcaggccatt cctaccaaag gaagaaaggc tggtctctcc acccctgta
                                                                       180
ggaaaggcct gccttgtaag acaccacaat ncggctgaat ctnaagtctt gtgttttact
                                                                       240
aatggaaaaa aaaaataaac aanaggtttt gttctcatgg ctgcccaccg cagcctggca
                                                                       300
ctaaaacanc ccagcgctca cttctgcttg ganaaatatt ctttgctctt ttggacatca
                                                                       360
```

```
ggcttgatgg tatcactgcc acntttccac ccagctgggc ncccttcccc catntttgtc
                                                                        420
antganctgg aaggeetgaa nettagtete caaaagtete ngeecacaag aceggeeace
                                                                        480
aggggangtc ntttncagtg gatctgccaa anantacccn tatcatcnnt gaataaaaag
                                                                        540
gcccctgaac ganatgcttc cancancctt taagacccat aatcctngaa ccatggtgcc
                                                                        600
cttccggtct gatccnaaag gaatgttcct gggtcccant ccctcctttg ttncttacgt
                                                                        660
tgtnttggac contgetngn atnacceaan tganatecec ngaagcacce tncccctggc
                                                                        720
atttganttt cntaaattct ctgccctacn nctgaaagca cnattccctn ggcnccnaan
                                                                       780
ggngaactca agaaggtctn ngaaaaacca cncn
                                                                        814
      <210> 37
      <211> 760
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1) ... (760)
      <223> n = A,T,C or G
      <400> 37
gcatgctgct cttcctcaaa gttgttcttg ttgccataac aaccaccata ggtaaagcgg
                                                                        60
gcgcagtgtt cgctgaaggg gttgtagtac cagcgcggga tgctctcctt gcagagtcct
                                                                       120 .
gtgtctggca ggtccacgca atgccctttg tcactgggga aatggatgcg ctggagctcg
                                                                       180
tenaanceae tegtgtattt tteacangea geeteeteeg aagenteegg geagttgggg
                                                                       240
gtgtcgtcac actccactaa actgtcgatn cancagccca ttgctgcagc ggaactgggt
                                                                       300
gggctgacag gtgccagaac acactggatn ggcctttcca tggaagggcc tgggggaaat
                                                                       360 .
cncctnance caaactgeet etcaaaggee acettgeaca ceeegacagg etagaaatge
                                                                       420
actettette ccaaaggtag ttgttettgt tgeccaagea neetecanea aaccaaaane
                                                                       480
ttgcaaaatc tgctccgtgg gggtcatnnn taccanggtt ggggaaanaa acccggcngn
                                                                       540
gancencett gtttgaatge naaggnaata atecteetgt ettgettggg tggaanagea
                                                                       600
caattgaact gttaacnttg ggccgngttc cnctngggtg gtctgaaact aatcaccgtc
                                                                       660
actggaaaaa ggtangtgcc ttccttgaat tcccaaantt cccctngntt tgggtnnttt
                                                                       720
ctcctctncc ctaaaaatcg tnttccccc ccntanggcg
                                                                       760
      <210> 38
      <211> 724
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(724)
      \langle 223 \rangle n = A,T,C or G
      <400> 38
ttttttttt tttttttt tttttttt tttttaaaaa ccccctccat tgaatgaaaa
                                                                        60
cttccnaaat tgtccaaccc cctcnnccaa atnnccattt ccgggggggg gttccaaacc
                                                                       120
caaattaatt ttgganttta aattaaatnt tnattngggg aanaanccaa atgtnaagaa
                                                                       180
aatttaaccc attatnaact taaatnootn gaaaccontg gnttocaaaa atttttaacc
                                                                      240
cttaaatccc tccgaaattg ntaanggaaa accaaattcn cctaaggctn tttgaaggtt
                                                                       300
ngatttaaac ccccttnant tnttttnacc cnngnctnaa ntatttngnt tccggtgttt.
                                                                      360
tectnttaan entnggtaac teeegntaat gaannneet aanceaatta aacegaattt
                                                                       420
tttttgaatt ggaaattccn ngggaattna ccggggtttt tcccntttgg gggccatncc
                                                                       480
cccnctttcg gggtttgggn ntaggttgaa tttttnnang ncccaaaaaa ncccccaana
                                                                       540
aaaaaactcc caagnnttaa ttngaatntc ccccttccca ggccttttgg gaaaggnggg
                                                                       600
```

tttntggggg congggantt cnttccccn ttnccnccc cccccnggt aaanggttat

```
ngnntttggt ttttgggccc cttnanggac cttccggatn gaaattaaat ccccgggncg
                                                                        720
gccg
                                                                        724
       <210> 39
       <211> 751
      <212> DNA
       <213> Homo sapien
      <220>
      <221> misc feature
      <222> (1)...(751)
      <223> n = A,T,C or G
      <400> 39
ttttttttt tttttctttg ctcacattta atttttattt tgatttttt taatgctgca
                                                                        60
caacacaata tttatttcat ttgtttcttt tatttcattt tatttgtttg ctgctgctgt
                                                                       120
tttatttatt tttactgaaa gtgagaggga acttttgtgg cctttttcc ttttctgta
                                                                       180
ggccgcctta agctttctaa atttggaaca tctaagcaag ctgaanggaa aagggggttt
                                                                       240
cgcaaaatca ctcgggggaa nggaaaggtt gctttgttaa tcatgcccta tggtgggtga
                                                                       300
ttaactgctt gtacaattac ntttcacttt taattaattg tgctnaangc tttaattana
                                                                       360
cttgggggtt ccctccccan accaaccccn ctgacaaaaa gtgccngccc tcaaatnatg
                                                                       420
teceggennt entigaaaca caengengaa ngtteteatt nteceenene cagginaaaa
                                                                       480
tgaagggtta ccatntttaa cnccacctcc acntggcnnn gcctgaatcc tcnaaaancn
                                                                       540
eceteaanen aattnetnng eceeggtene gentnngtee eneceggget eegggaantn
                                                                       600
cacececnga annenntnne naacnaaatt eegaaaatat teeenntene teaatteeee
                                                                       660
cnnagactnt cctcnncnan cncaattttc ttttnntcac gaacncgnnc cnnaaaatgn
                                                                       720
nnnncncctc cnctngtccn naatcnccan c
                                                                       751
      <210> 40
      <211> 753
    : <212> DNA
    <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(753)
      <223> n = A,T,C or G
      <400> 40
gtggtatttt ctgtaagatc aggtgttcct ccctcgtagg tttagaggaa acaccctcat
                                                                        60
agatgaaaac ccccccgaga cagcagcact gcaactgcca agcagccggg gtaggagggg
                                                                      120
cgecctatgc acagctgggc ccttgagaca gcagggcttc gatgtcaggc tcgatgtcaa
                                                                      180
tggtctggaa gcggcggctg tacctgcgta ggggcacacc gtcagggccc accaggaact
                                                                      240
teteaaagtt ceaggeaacn tegttgegae acaeeggaga eeaggtgatn agettggggt
                                                                      300
cggtcataan cgcggtggcg tcgtcgctgg gagctggcag ggcctcccgc aggaaggcna
                                                                      360
ataaaaggtg cgccccgca ccgttcanct cgcacttctc naanaccatg angttgggct
                                                                      420
cnaacccacc accanneegg actteettga nggaatteec aaatetette gntettggge
                                                                      480
ttctnctgat gecetanctg gttgeeengn atgecaanca neceeaance eeggggteet
                                                                      540
aaancaccon cotcotontt toatotgggt tnttntcccc ggaccntggt toctotcaag
                                                                      600
ggancccata tetenacean tacteacent neceeecent gnnacecane ettetanngn
                                                                      660
ttcccncccg ncctctggcc cntcaaanan gcttncacna cctgggtctg ccttccccc
                                                                      720
tnccctatct gnaccccncn tttgtctcan tnt
                                                                      753
```

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<211> 341
      <212> DNA
      <213> Homo sapien
      <400> 41
actatateca teacaacaga catgetteat eccatagaet tettgacata getteaaatg
agtgaaccca tccttgattt atatacatat atgttctcag tattttggga gcctttccac
                                                                      120
ttctttaaac cttgttcatt atgaacactg aaaataggaa tttgtgaaga gttaaaaagt
                                                                      180
tatagettgt ttacgtagta agtttttgaa gtctacattc aatccagaca cttagttgag
                                                                      240
tgttaaactg tgatttttaa aaaatatcat ttgagaatat tctttcagag gtattttcat
                                                                      300
ttttactttt tgattaattg tgttttatat attagggtag t
                                                                      341
      <210> 42
      <211> 101
      <212> DNA
      <213> Homo sapien
      <400> 42
acttactgaa tttagttctg tgctcttcct tatttagtgt tgtatcataa atactttgat
gtttcaaaca ttctaaataa ataattttca gtggcttcat a
      <210> 43
      <211> 305
      <212> DNA
      <213> Homo sapien
      <400> 43
acatetttgt tacagtetaa gatgtgttet taaateacea tteetteetg gteeteacee
tccagggtgg tctcacactg taattagagc tattgaggag tctttacagc aaattaagat
                                                                     120
tcagatgcct tgctaagtct agagttctag agttatgttt cagaaagtct aagaaaccca
                                                                     180
cctcttgaga ggtcagtaaa gaggacttaa tatttcatat ctacaaaatg accacaggat
                                                                     240
tggatacaga acgagagtta tcctggataa ctcagagctg agtacctgcc cgggggccgc
                                                                     300
tcgaa
      <210> 44
      <211> 852
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(852)
     <223> n = A,T,C or G
      <400> 44
acataaatat cagagaaaag tagtotttga aatatttacg tocaggagtt otttgtttot
                                                                      60
gattatttgg tgtgtgtttt ggtttgtgtc caaagtattg gcagcttcag ttttcatttt
                                                                     120
ctctccatcc tcgggcattc ttcccaaatt tatataccag tcttcgtcca tccacacgct
ccagaatttc tcttttgtag taatatctca tagctcggct gagcttttca taggtcatgc
tgctgttgtt cttcttttta ccccatagct gagccactgc ctctgatttc aagaacctga
                                                                     300
agacgccctc agatcggtct tcccatttta ttaatcctgg gttcttgtct gggttcaaga
                                                                     360
ggatgtcgcg gatgaattcc cataagtgag tccctctcgg gttgtgcttt ttggtgtggc
                                                                     420
acttggcagg ggggtcttgc tcctttttca tatcaggtga ctctgcaaca ggaaggtgac
                                                                     480
tggtggttgt catggagatc tgagcccggc agaaagtttt gctgtccaac aaatctactg
                                                                     540
tgctaccata gttggtgtca tataaatagt tctngtcttt ccaggtgttc atgatggaag
```

```
gctcagtttg ttcagtcttg acaatgacat tgtgtgtgga ctggaacagg tcactactgc
                                                                        660
 actggccgtt ccacttcaga tgctgcaagt tgctgtagag gagntgcccc gccgtccctg
                                                                        720
 ccgcccgggt gaactcctgc aaactcatgc tgcaaaggtg ctcgccgttg atgtcgaact
                                                                        780
 cntggaaagg gatacaattg gcatccagct ggttggtgtc caggaggtga tggagccact
                                                                        840
 cccacacctg gt
                                                                        852
       <210> 45
       <211> 234
       <212> DNA : . . . .
       <213> Homo sapien
       <400> 45
 acaacagacc cttgctcgct aacgacctca tgctcatcaa gttggacgaa tccgtgtccg
                                                                         60
 agtetgacae cateeggage ateageattg ettegeagtg ceetacegeg gggaactett
                                                                        120
 geetegttte tggetggggt etgetggega aeggeagaat geetaeegtg etgeagtgeg
                                                                        180
 tgaacgtgtc ggtggtgtct gaggaggtct gcagtaagct ctatgacccg ctgt
                                                                        234
       <210> 46
       <211> 590.
       <212> DNA
       <213> Homo sapien
       <220>
       <221> misc_feature
       <222> (1)...(590)
       <223> n = A,T,C or G
      <400> 46
actttttatt taaatgttta taaggcagat ctatgagaat gatagaaaac atggtgtgta
                                                                        60
atttgatagc aatattttgg agattacaga gttttagtaa ttaccaatta cacagttaaa
                                                                       120
aagaagataa tatattccaa gcanatacaa aatatctaat gaaagatcaa ggcaggaaaa
                                                                       180
tgantataac taattgacaa tggaaaatca attttaatgt gaattgcaca ttatccttta
                                                                       240
aaagctttca aaanaaanaa ttattgcagt ctanttaatt caaacagtgt taaatggtat
                                                                       300
caggataaan aactgaaggg canaaagaat taattttcac ttcatgtaac ncacccanat
                                                                       360
ttacaatggc ttaaatgcan ggaaagca gtggaagtag ggaagtantc aaggtctttc
                                                                       420
tggtctctaa tctgccttac tctttgggtg tggctttgat cctctggaga cagctgccag
                                                                       480
ggctcctgtt atatccacaa tcccagcagc aagatgaagg gatgaaaaag gacacatgct
                                                                       540
gccttccttt gaggagactt catctcactg gccaacactc agtcacatgt
      <210> 47
      <211> 774
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1) ... (774)
      <223> n = A,T,C or G
      <400> 47
acaagggggc ataatgaagg agtggggana gattttaaag aaggaaaaaa aacgaggccc
                                                                       60
tgaacagaat tttcctgnac aacggggctt caaaataatt ttcttgggga ggttcaagac
                                                                      120
getteactge ttgaaactta aatggatgtg ggacanaatt ttetgtaatg accetgaggg
                                                                      180
cattacagac gggactctgg gaggaaggat aaacagaaag gggacaaagg ctaatcccaa
                                                                      240
aacatcaaag aaaggaaggt ggcgtcatac ctcccagcct acacagttct ccagggctct
                                                                      300
```

cctcatcct ggaggacgac agtggaggaa ctggctctg gtcttcagcc cccagctctg ccacactcct tgaacacaca tccccaggtt cctacttccg agatgccttg ctccctgcag acggcatggg aagcctttct gacttgcctg ttccccactc cttagaggca agatagggtg aggctgctgg cttcaaattn tggctcattt tcacttctat gggcntcatt ttgttctacc	gaagcccacc atattcctgg cctgtcaaaa attactccag gttaagagta acgagctatg	ctctgctgat acatggctga tcccactcac catcttggaa gggctggacc ggaccttggg	cctgcgtggc acctcctatt cctccaaacc caatccctga acttggagcc caagtnatct	360 420 480 540 600 660 720
<210> 48				
<211> 124				
<212> DNA		. •	· · · ·	
<213> Homo sapien	•			
<220>				
<221> misc_feature				
<222> (1) (124)	•			
<223> n = A,T,C or G	·			• • •
			1. 1.1.	
<400> 48			• • •	•
canaaattga aattttataa aaaggcattt				60
ttgcaantat anaaatgtgt cataaattat tggt	aacyccccc	aactacaget	caacgcaact	120
		* * * * * * * * * * * * * * * * * * * *		124
<210> 49				•
<211> 147	•.			
<212> DNA			6 tw	
<213> Homo sapien				•
				•
<220>	• • •			٠.
<221> misc_feature <222> (1)(147)				
<223> n = A,T,C  or  G				
			:	
<400> 49	•		•	
gccgatgcta ctattttatt gcaggaggtg	ggggtgtttt	tattattctc	tcaacagctt	60
tgtggctaca ggtggtgtct gactgcatna	aaaanttttt	tacgggtgat	tgcaaaaatt	120
ttagggcacc catatcccaa gcantgt			-	147
-210- 50		•		•
<210> 50 <211> 107				
<212> DNA				
<213> Homo sapien		•	•	
		•		
<400> 50			•	
acattaaatt aataaaagga ctgttggggt	tctgctaaaa	cacatggctt	gatatattgc	60
atggtttgag gttaggagga gttaggcata	tgttttggga	gaggggt	. *	107
210. 51	•			
<210> 51 <211> 204	•			•
<211> 204 <212> DNA				
<212> bNA <213> Homo sapien	• .			
Table 1000 DapaGH			•	٠.
<400> 51	•			
gtcctaggaa gtctagggga cacacgactc	tggggtcacg	gggccgacac	acttgcacgg	60
	•			

```
cgggaaggaa aggcagagaa gtgacaccgt cagggggaaa tgacagaaag gaaaatcaag
                                                                         120
 gccttgcaag gtcagaaagg ggactcaggg cttccaccac agccctgccc cacttggcca
                                                                         180
 cctccctttt gggaccagca atgt
                                                                         204
        <210> 52
        <211> 491
        <212> DNA
        <213> Homo sapien
       <220>
       <221> misc_feature
       <222> (1)...(491)
       <223> n = A, T, C or G
       <400> 52
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                                                                         60
 gggtattttc caaaagacta aagagataac tcaggtaaaa agttagaaat gtataaaaca
                                                                        120
 ccatcagaca ggtttttaaa aaacaacata ttacaaaatt agacaatcat ccttaaaaaa
                                                                        180
 aaaacttctt gtatcaattt cttttgttca aaatgactga cttaantatt tttaaatatt
                                                                        240
 tcanaaacac ttcctcaaaa attttcaana tggtagcttt canatgtncc ctcagtccca
                                                                        300
 atgttgctca gataaataaa tctcgtgaga acttaccacc caccacaagc tttctggggc
                                                                        360
 atgcaacagt gtctttctt tnctttttct ttttttttt ttacaggcac agaaactcat
                                                                        420
 caattttatt tggataacaa agggtctcca aattatattg aaaaataaat ccaagttaat
                                                                        480
 atcactcttg t
                                                                        491
       <210> 53
       <211> 484
       <212> DNA
       <213> Homo sapien
       <220>
       <221> misc_feature
       <222> (1)...(484)
      <223> n = A, T, C or G
      <400> 53
acataattta gcagggctaa ttaccataag atgctattta ttaanaggtn tatgatctga
gtattaacag ttgctgaagt ttggtatttt tatgcagcat tttctttttg ctttgataac
                                                                       120
actacagaac ccttaaggac actgaaaatt agtaagtaaa gttcagaaac attagctgct
                                                                       180
caatcaaatc tctacataac actatagtaa ttaaaacgtt aaaaaaaagt gttgaaatct
                                                                       240
gcactagtat anaccgctcc tgtcaggata anactgcttt ggaacagaaa gggaaaaanc
                                                                       300
agetttgant ttetttgtge tgatangagg aaaggetgaa ttacettgtt geeteteeet
                                                                       360
aatgattggc aggtcnggta aatnccaaaa catattccaa ctcaacactt cttttccncg
                                                                       420
tancttgant ctgtgtattc caggancagg cggatggaat gggccagccc ncggatgttc
                                                                       480
cant
                                                                       484
      <210> 54
      <211> 151
      <212> DNA
      <213> Homo sapien
      <400> 54
actaeacctc gtgcttgtga actccataca gaaaacggtg ccatccctga acacggctgg
ccactgggta tactgctgac aaccgcaaca acaaaaacac aaatccttgg cactggctag
                                                                       120
tctatgtcct ctcaagtgcc tttttgtttg t
```

<213> Homo sapien

<210> 55	,			
<211> 91				
<212> DNA				
<213> Homo sapien				
	•		***	
<400> 55				-
acctggettg teteegggtg gtteeeggeg		tccccagaac	ggacactttc	60
gecetecagt ggatactega gecaaagtgg	t			91
210 56			•	
<210> 56				
<211> 133				
<212> DNA				
<213> Homo sapien			•	
<400> 56				
ggcggatgtg cgttggttat atacaaatat	atcatttat	at a sagge at	tanatatas	
tggatttttg gtatctgtgg gttgggggga				60
aagggacaac tgt	cggcccagga	accaacaccc	Catygatace	120
22322222				133
<210> 57				
<211> 147				
<212> DNA				
<213> Homo sapien	•			
<del>-</del> ·		•		
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<221> misc_feature				٠.
<222> (1)(147)			:	
<223> n = A,T,C or G				•
			· .	
<400> 57			••	
actetggaga acetgageeg etgeteegee				60
gactgggagc tgagcccttc cctttgcgcc	tgcctcagag	gattgttgcc	gacntgcana	120
tctcantggg ctggatncat gcagggt				147
000 50			* * * * * * * * * * * * * * * * * * * *	
<210> 58		: :		
<211> 198				
<212> DNA	•		- •	
<213> Homo sapien				
<220>		•		
<221> misc_feature		• .		
<222> (1)(198)				
$\langle 222 \rangle$ (1)(136) $\langle 223 \rangle$ n = A,T,C or G	:		•	
(223) II = A,1,0 OI G	-			
<400> 58				
acagggatat aggtttnaag ttattgtnat	totaaaatac	attgaattt	Ctotatacto	60
tgattacata catttatcct ttaaaaaaga				120
atttaccaat gagttacctt gtaaatgaga				180
ttgacttcta agtttggt	-goodeyata	Jeacegaare	ccaaccagee	198
				190
<210> 59				
<211> 330	•	•		•
<212> DNA	•		4.	

٤.

<400> 59	
acaacaaatg ggttgtgagg aagtettate agcaaaactg gtgatggeta etgaaaagat	60
Ccattgaaaa ttatcattaa tgattttaaa tgacaaqtta tcaaaaactc actcaatttt	120
Caccigiget agetigetaa aatgggagti aactetagag caaatatagi atettergaa	180
tacagtcaat aaatgacaaa gccagggcct acaggtggtt tccagacttt ccagaccag	240
cagaaggaat ctattttatc acatggatct ccgtctgtgc tcaaaatacc taatgatatt	
tttcgtcttt attggacttc tttgaagagt	300
	330
<210> 60	
<211> 175	
<212> DNA	
<213> Homo sapien	
<400> 60	
acceptagges cettetacat teetgacgge teetteacca acatetggtt etacttegge	60
gregregger cerrecter careereate cagerggree tectearea ettracase	120
tcctggaacc agcggtggct gggcaaggcc gaggagtgcg attcccgtgc ctggt	175
	1/3
<210> 61	
<211> 154	
<212> DNA	•
<213> Homo sapien	
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accccacttt tcctcctgtg agcagtctgg acttctcact gctacatgat gagggtgagt	60
gyrigitget etteaaeagt atecteeeet tteeggatet getgageegg acaggagtge	120
LYVALLULAU AUCCCCCCCCCC CCCCCCCCCCCCCCCCCCC	154
-210. 62	
<210> 62 <211> 30	
<211> 30 <212> DNA	٠
<213> Homo sapien	
<400> 62	
cgctcgagcc ctatagtgag tcgtattaga	
-goodgagoo ccacagogag cogcactaga	30
<210> 63	
<211> 89	
<212> DNA	
<213> Homo sapien	
<400> 63	
acaagtcatt tcagcaccct ttgctcttca aaactgacca tcttttatat ttaatgcttc	
Etgtatgaat aaaaatggtt atgtcaagt	60
	89
<210> 64	
<211> 97	
<212> DNA	
<213> Homo sapien	
<400> 64	
ACCOGNATIAN CTONOTCOMO REGETARATA TARRESTA TARRESTA	cò
lacadida iccadatta atecttarat otaras	60
	97

```
<210> 65
      <211> 377
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1) ... (377)
      <223> n = A,T,C or G
      <400> 65
acaacaanaa ntecettett taggecaetg atggaaacet ggaaceeet tttgatggea
                                                                         60
gcatggcgtc ctaggccttg acacagcggc tggggtttgg gctntcccaa accgcacacc
                                                                        120
ccaaccctgg tctacccaca nttctggcta tgggctgtct ctgccactga acatcagggt
                                                                        180
tcggtcataa natgaaatcc caanggggac agaggtcagt agaggaagct caatgagaaa
                                                                        240
ggtgctgttt gctcagccag aaaacagctg cctggcattc gccgctgaac tatqaacccq
                                                                        300
tgggggtgaa ctaccccan gaggaatcat gcctgggcga tgcaanggtg ccaacaggag
                                                                        360
gggcgggagg agcatgt
                                                                        377
      <210> 66
      <211> 305
      <212> DNA
      <213> Homo sapien
      <400> 66
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                                                                       60
agaaccegtg tgccccttcc caccatatec accetegete catetttgaa etcaaacaeg
                                                                       120
aggaactaac tgcaccctgg tcctctcccc agtccccagt tcaccctcca tccctcacct
                                                                       180
tcctccactc taagggatat caacactgcc cagcacaggg gccctgaatt tatgtggttt
                                                                       240
ttatatattt tttaataaga tgcactttat gtcatttttt aataaagtct gaagaattac
                                                                       300
tgttt
                                                                       305
      <210> 67
      <211> 385
      <212> DNA
      <213> Homo sapien
      <400> 67
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                                                                        60
ggtcggacca gccacatctc atgtgcaaga ttgcccagca gacatcaggt ctgagagttc
                                                                       120
cccttttaaa aaaggggact tgcttaaaaa agaagtctag ccacgattgt gtagagcagc
                                                                       180
tgtgctgtgc tggagattca cttttgagag agttctcctc tgagacctga tctttagagg
                                                                       240
ctgggcagtc ttgcacatga gatggggctg gtctgatctc agcactcctt agtctgcttg
                                                                       300
cctctcccag ggccccagcc tggccacacc tgcttacagg gcactctcag atgcccatac
                                                                       360
catagtttct gtgctagtgg accgt
                                                                       385
      <210> 68
      <211> 73
      <212> DNA
      <213> Homo sapien
      <400> 68
acttaaccag atatatttt accccagatg gggatattct ttgtaaaaaa tgaaaataaa
                                                                        60
gtttttttaa tgg
                                                                        73
```

```
<210> 69
       <211> 536
       <212> DNA
       <213> Homo sapien
       <220>
       <221> misc_feature
       <222> (1)...(536)
       <223> n = A, T, C or G
       <400> 69
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                                                                         60
 tecagettig igeteigeet eigaggagae eaiggeeeag eaictgagta eeeigeiget
                                                                         120
cctgctggcc accctagctg tggccctggc ctggagcccc aaggaggagg ataggataat
                                                                         180
cccgggtggc atctataacg cagacctcaa tgatgagtgg gtacagcgtg cccttcactt
                                                                         240
cgccatcagc gagtataaca aggccaccaa agatgactac tacagacgtc cgctgcgggt
                                                                         300
actaagagcc aggcaacaga ccgttggggg ggtgaattac ttcttcgacg tagaggtggg
                                                                        360
ccgaaccata tgtaccaagt cccagcccaa cttggacacc tgtgccttcc atgaacagcc
                                                                        420
agaactgcag aagaaacagt tgtgctcttt cgagatctac gaagttccct ggggagaaca
                                                                        480
gaangtccct gggtgaaatc caggtgtcaa gaaatcctan ggatctgttg ccaggc
                                                                        536
      <210> 70
      <211> 477
      <212> DNA
      <213> Homo sapien
     <400> 70
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                                                                         60
tcacttccac tccataacgc tcctcatact aggcctacta accaacacac taaccatata
                                                                        120
ccaatgatgg cgcgatgtaa cacgagaaag cacataccaa ggccaccaca caccacctgt
                                                                        180
ccaaaaaggc cttcgatacg ggataatcct atttattacc tcagaagttt ttttcttcgc
                                                                        240
agggattttt ctgagccttt taccactcca gcctagcccc tacccccaa ctaggagggc
                                                                        300
actggccccc aacaggcatc accccgctaa atcccctaga agtcccactc ctaaacacat
                                                                        360
ccgtattact cgcatcagga gtatcaatca cctgagctca ccatagtcta atagaaaaca
                                                                        420
accgaaacca aattattcaa agcactgctt attacaattt tactgggtct ctattt
                                                                        477
      <210> 71
      <211> 533
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1) ... (533)
      \langle 223 \rangle n = A,T,C or G
      <400> 71
agagetatag gtacagtgtg ateteagett tgcaaacaca ttttetacat agatagtact
                                                                        60
aggtattaat agatatgtaa agaaagaaat cacaccatta ataatggtaa gattggttta
                                                                       120
tgtgatttta gtggtatttt tggcaccctt atatatgttt tccaaacttt cagcagtgat
                                                                       180
attatttcca taacttaaaa agtgagtttg aaaaagaaaa tctccagcaa gcatctcatt
                                                                       240
taaataaagg tttgtcatct ttaaaaaatac agcaatatgt gactttttaa aaaagctgtc
                                                                       300
aaataggtgt gaccctacta ataattatta gaaatacatt taaaaacatc gagtacctca
                                                                       360
agtcagtttg ccttgaaaaa tatcaaatat aactcttaga gaaatgtaca taaaagaatg
                                                                       420
cttcgtaatt ttggagtang aggttccctc ctcaattttg tattttaaa aagtacatgg
                                                                       480
taaaaaaaaa aattcacaac agtatataag gctgtaaaat gaagaattct gcc
                                                                       533
```

```
<210> 72
      <211> 511
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1) ... (511)
      <223> n = A,T,C or G
      <400> 72
tattacggaa aaacacacca cataattcaa ctancaaaga anactgcttc agggcgtgta
                                                                     60
aaatgaaagg cttccaggca gttatctgat taaagaacac taaaagaggg acaaggctaa
aagccgcagg atgtctacac tatancaggc gctatttggg ttggctggag gagctgtgga
                                                                    180
aaacatggan agattggtgc tgganatcgc cgtggctatt cctcattgtt attacanagt
                                                                    240
gaggttetet gtgtgeecac tggtttgaaa accgttetne aataatgata gaatagtaca
                                                                    300
cacatgagaa ctgaaatggc ccaaacccag aaagaaagcc caactagatc ctcagaanac
                                                                    360
gcttctaggg acaataaccg atgaagaaaa gatggcctcc ttgtgccccc gtctgttatg
                                                                    420
atttctctcc attgcagcna naaacccgtt cttctaagca aacncaggtg atgatggcna
                                                                    480
aaatacaccc cctcttgaag naccnggagg a
      <210> 73
      <211> 499
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(499)
      <223> n = A,T,C or G
      <400> 73
cagtgccagc actggtgcca gtaccagtac caataacagt gccagtgcca gtgccagcac
                                                                    60
cagtggtggc ttcagtgctg gtgccagcct gaccgccact ctcacatttg ggctcttcgc
                                                                    120
tggccttggt ggagctggtg ccagcaccag tggcagctct ggtgcctgtg gtttctccta
                                                                    180
caagtgagat titagatatt gitaatccig ccagictitc tcttcaagcc agggigcatc
                                                                    240
ctcagaaacc tactcaacac agcactctag gcagccacta tcaatcaatt gaagttgaca
                                                                    300
360
antitagagg gecegittaa accegetgat cageetegae tgtgeettet antiqeeage
                                                                    420
catctgttgt ttgcccctcc cccgntgcct tccttgaccc tggaaagtgc cactcccact
                                                                    480
gtcctttcct aantaaaat
                                                                    499
     <210> 74
     <211> 537
     <212> DNA
     <213> Homo sapien
     <220>
     <221> misc_feature
     <222> (1)...(537)
     <223> n = A,T,C or G
     <400> 74
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tttcatagga gaacacactg aggagatact tgaagaattt ggattcagcc gcgaagagat

```
ttatcagctt aactcagata aaatcattga aagtaataag gtaaaagcta gtctctaact
                                                                          120
  tccaggccca cggctcaagt gaatttgaat actgcattta cagtgtagag taacacataa
                                                                          180
 cattgtatgc atggaaacat ggaggaacag tattacagtg tcctaccact ctaatcaaga
                                                                          240
 aaagaattac agactctgat tctacagtga tgattgaatt ctaaaaatgg taatcattag
                                                                          300
 ggcttttgat ttataanact ttgggtactt atactaaatt atggtagtta tactgccttc
                                                                          360
 cagtttgctt gatatatttg ttgatattaa gattcttgac ttatattttg aatgggttct
                                                                          420
 actgaaaaan gaatgatata ttcttgaaga catcgatata catttattta cactcttgat
                                                                          480
 tctacaatgt agaaaatgaa ggaaatgccc caaattgtat ggtgataaaa gtcccgt
                                                                         537
        <210> 75
       <211> 467
       <212> DNA
       <213> Homo sapien
       <220>
       <221> misc_feature.
       <222> (1) ... (467)
       <223> n = A,T,C \text{ or } G
     <400> 75
 caaanacaat tgttcaaaag atgcaaatga tacactactg ctgcagctca caaacacctc
                                                                          60
 tgcatattac acgtacctcc tectgetect caagtagtgt ggtctatttt gccatcatca
                                                                         120
 cctgctgtct gcttagaaga acggctttct gctgcaangg agagaaatca taacagacgg
                                                                         180
 tggcacaagg aggccatctt ttcctcatcg gttattgtcc ctagaagegt cttctgagga
                                                                         240
 totagttggg ctttctttct gggtttgggc catttcantt ctcatgtgtg tactattcta
                                                                         300
 tcattattgt ataacggttt tcaaaccngt gggcacncag agaacctcac tctgtaataa
                                                                         360
 caatgaggaa tagccacggt gatctccagc accaaatctc tccatgttnt tccagagctc
                                                                         420
 ctccagccaa cccaaatagc cgctgctatn gtgtagaaca tccctgn
                                                                         467
       <210> 76
       <211> 400
       <212> DNA
       <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1) ... (400)
      \langle 223 \rangle n = A,T,C or G
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                                                                         60
tetetette tggcetggag getatecage gtactecaaa gatteaggtt tacteacgte
                                                                        120
atccagcaga gaatggaaag tcaaatttcc tgaattgcta tgtgtctggg tttcatccat
                                                                        180
ccgacattga agttgactta ctgaagaatg gagagagaat tgaaaaagtg gagcattcag
                                                                        240
acttgtcttt cagcaaggac tggtctttct atctcttgta ctacactgaa ttcacccca
                                                                        300
ctgaaaaaga tgagtatgcc tgccgtgtga accatgtgac tttgtcacag cccaagatng
                                                                        360
ttnagtggga tcganacatg taagcagcan catgggaggt
                                                                        400
      <210> 77
      <211> 248
      <212> DNA
      <213> Homo sapien
      <400> 77
ctggagtgcc ttggtgtttc aagcccctgc aggaagcaga atgcaccttc tgaggcacct
                                                                         60
```

ccagctgccc cggcggggga tgcgaggctc	ggagcaccct	tgcccggctg	tgattgctgc	120
caggeactgt teateteage ttttetgtee				180
gttcatatct ggagcctgat gtcttaacga	acaaaggccc	Catgeteeae	ccgaaaaaaa	240
aaaaaaa				248
•			•	
<210> 78				
<211> 201				_
<212> DNA	•	•		•
<213> Homo sapien			F 7 17 =	
<213> Nomo Saptem		•	•	
			•	٠.
<400> 78				
actagtccag tgtggtggaa ttccattgtg	ttgggcccaa	cacaatggct	acctttaaca	60
tcacccagac cccgccctgc ccgtgcccca	cactactact	aacgacagta	tgatgcttac	120
tctgctactc ggaaactatt tttatgtaat				180
	caacgcacgc	cccccgccc	acadacycci	
gatttaaaaa aaaaaaaaa a		•		201
<210> 79				
<211> 552				
<212> DNA	•	•		
<213> Homo sapien				
Tabe nome bapten		. •		
<220>	•		the second of the	
<221> misc_feature	• •			
<222> (1)(552)				•
<223> n = A, T, C  or  G				
<400> 79	•			
	anact nonet			
tccttttgtt aggtttttga gacaacccta				60
tttaggcagt gctagtaatt tcctcgtaat				120
cctctttctt ctgaagatta atgaagttga				180 .
tgtgatagta taagtatcta agtgcagatg	aaagtgtgtt	atatatatcc	attcaaaatt	240
atgcaagtta gtaattactc agggttaact	aaattacttt	aatatgctgt	tgaacctact	300
ctgttccttg gctagaaaaa attataaaca				360
taatattcta tgttctaaaa gttgggctat				420
ttcccaggaa tatggggttc atttatgaat				480
cngttttggt taatacgtta atatgtcctn	aatnaacaag	gcntgactta	tttccaaaaa	540
aaaaaaaaa aa				<b>552</b> .
			···	
<210> 80			<b></b>	
<211> 476				
<212> DNA				
	• •			
<213> Homo sapien			** * * * * *	
	•			
<220>		, , ,	•	
<221> misc_feature				
		•		
<222> (1)(476)				
<222> (1)(476) <223> n = A.T.C or G			en e	
<222> (1)(476) <223> n = A,T,C or G				
<223> n = A,T,C  or  G				
<223> $n = A, T, C \text{ or } G$ <400> 80				
<223> n = A,T,C or G  <400> 80 acagggattt gagatgctaa ggccccagag				60
<223> n = A,T,C or G  <400> 80 acagggattt gagatgctaa ggccccagag				60 120
<223> n = A,T,C or G  <400> 80 acagggattt gagatgctaa ggccccagag ggggaaaatg gggcctagaa gttacagagc	atctagctgg	tgcgctggca	cccctggcct	120
<223> n = A,T,C or G  <400> 80 acagggattt gagatgctaa ggccccagag ggggaaaatg gggcctagaa gttacagagc cacacagact cccgagtagc tgggactaca	atctagctgg ggcacacagt	tgcgctggca cactgaagca	cccctggect ggccctgttt	120 180
<pre>&lt;223&gt; n = A,T,C or G  &lt;400&gt; 80 acagggattt gagatgctaa ggccccagag ggggaaaatg gggcctagaa gttacagagc cacacagact cccgagtagc tgggactaca gcaattcacg ttgccacctc caacttaaac</pre>	atctagctgg ggcacacagt attcttcata	tgcgctggca cactgaagca tgtgatgtcc	cccctggect ggccctgttt ttagtcacta	120 180 240
<pre>&lt;223&gt; n = A,T,C or G  &lt;400&gt; 80 acagggattt gagatgctaa ggccccagag ggggaaaatg gggcctagaa gttacagagc cacacagact cccgagtagc tgggactaca gcaattcacg ttgccacctc caacttaaac aggttaaact ttcccaccca gaaaaggcaa</pre>	atctagctgg ggcacacagt attcttcata cttagataaa	tgcgctggca cactgaagca tgtgatgtcc atcttagagt	ccctggcct ggccctgttt ttagtcacta actttcatac	120 180 240 300
<pre>&lt;223&gt; n = A,T,C or G  &lt;400&gt; 80 acagggattt gagatgctaa ggccccagag ggggaaaatg gggcctagaa gttacagagc cacacagact cccgagtagc tgggactaca gcaattcacg ttgccacctc caacttaaac</pre>	atctagctgg ggcacacagt attcttcata cttagataaa	tgcgctggca cactgaagca tgtgatgtcc atcttagagt	ccctggcct ggccctgttt ttagtcacta actttcatac	120 180 240

```
tcttggcttt ctcaataaaa tctctatcca tctcatgttt aatttggtac gcntaaaaat
                                                                          420
   gctgaaaaaa ttaaaatgtt ctggtttcnc tttaaaaaaaa aaaaaaaaa aaaaaa
                                                                          476
         <210> 81
         <211> 232
         <212> DNA
         <213> Homo sapien
         <220>
         <221> misc_feature
         <222> (1)...(232)
         <223> n = A,T,C or G
         <400> 81
   tttttttttg tatgccntcn ctgtggngtt attgttgctg ccaccctgga ggagcccagt
                                                                           60
   ttettetgta tetttettt etgggggate tteetggete tgeeceteca tteecageet
                                                                          120
  ctcatcccca tcttgcactt ttgctagggt tggaggcgct ttcctggtag cccctcagag
                                                                          180
   actcagtcag cgggaataag tcctaggggt ggggggtgtg gcaagccggc ct
         <210> 82
         <211> 383
         <212> DNA
         <213> Homo sapien
        <220>
        <221> misc_feature
        <222> (1)...(383)
        <223> n = A,T,C or G
        <400> 82
 aggcgggagc agaagctaaa gccaaagccc aagaagagtg gcagtgccag cactggtgcc
                                                                          60
 agtaccagta ccaataacat gccagtgcca gtgccagcac cagtggtggc ttcagtgctg
                                                                         120
  gtgccagcct gaccgccact ctcacatttg ggctcttcgc tggccttggt ggagctggtg
                                                                         180
  ccagcaccag tggcagctct ggtgcctgtg gtttctccta caagtgagat tttagatatt
                                                                         240
  gttaatcctg ccagtctttc tcttcaagcc agggtgcatc ctcagaaacc tactcaacac
                                                                         300
  agcactctng gcagccacta tcaatcaatt gaagttgaca ctctgcatta aatctatttg
                                                                         360
. ccatttcaaa aaaaaaaaaa aaa
                                                                         383.
        <210> 83
        <211> 494
        <212> DNA
        <213> Homo sapien
        <220>
        <221> misc feature
        <222> (1)...(494)
        <223> n = A,T,C or G
        <400> 83
  accgaattgg gaccgctggc ttataagcga tcatgtcctc cagtattacc tcaacgagca
                                                                          60
  gggagatcga gtctatacgc tgaagaaatt tgacccgatg ggacaacaga cctgctcagc
                                                                         120
  ccatcctgct cggttctccc cagatgacaa atactctcga caccgaatca ccatcaagaa
                                                                         180
  acgetteaag gtgeteatga ceeageaace gegeeetgte etetgagggt cettaaactg
                                                                         240
  atgtetttte tgeeacetgt tacceetegg agaeteegta accaaactet teggaetgtg
                                                                         300
  agecetgatg cetttttgcc agecatacte tttggcntcc agtetetegt ggegattgat
                                                                         360
```

```
tatgettgtg tgaggeaate atggtggeat cacceatnaa gggaacacat ttgantttt
                                                                         420
tttcncatat tttaaattac naccagaata nttcagaata aatgaattga aaaactctta
                                                                         480
aaaaaaaaa aaaa
                                                                         494
      <210> 84
      <211> 380
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(380)
      \langle 223 \rangle n = A,T,C or G
      <400> 84
gctggtagcc tatggcgtgg ccacggangg gctcctgagg cacgggacag tgacttccca
                                                                          60
agtatectge geogegtett ctacegtece tacetgeaga tettegggea gattecceag
                                                                        120
gaggacatgg acgtggccct catggagcac agcaactgct cgtcggagcc cggcttctgg
                                                                         180
gcacaccctc ctggggccca ggcgggcacc tgcgtctccc agtatgccaa ctggctggtg
                                                                         240
gtgctgctcc tcgtcatctt cctgctcgtg gccaacatcc tgctggtcac ttgctcattg
                                                                        300
ccatgttcag ttacacattc ggcaaagtac agggcaacag cnatctctac tgggaaggcc
                                                                        360
agcgttnccg cctcatccgg
                                                                         380
      <210> 85
      <211> 481
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(481)
      \langle 223 \rangle n = A,T,C or G
      <400> 85
gagttagete etecacaace ttgatgaggt egtetgeagt ggeetetege tteatacege
tnccatcgtc atactgtagg tttgccacca cctcctgcat cttggggcgg ctaatatcca:
                                                                        120
ggaaactctc aatcaagtca ccgtcnatna aacctgtggc tggttctgtc ttccgctcgg
                                                                        180
tgtgaaagga tctccagaag gagtgctcga tcttccccac acttttgatg actttattga
                                                                        240
gtcgattctg catgtccagc aggaggttgt accagctctc tgacagtgag gtcaccagcc
                                                                        300
ctatcatgcc nttgaacgtg ccgaagaaca ccgagccttg tgtggggggt gnagtctcac
                                                                        360
ccagattctg cattaccaga nagccgtggc aaaaganatt gacaactcgc ccaggnngaa
                                                                        420
aaagaacacc teetggaagt getngeeget eetegteent tggtggnnge gentneettt
                                                                        480
t
                                                                        481
      <210> 86
      <211> 472
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc feature
      <222> (1)...(472)
      <223> n = A,T,C or G
      <400> 86
```

```
aacatcttcc tgtataatgc tgtgtaatat cgatccgatn ttgtctgctg agaattcatt
                                                                         60
 acttggaaaa gcaacttnaa gcctggacac tggtattaaa attcacaata tgcaacactt
                                                                        120
 taaacagtgt gtcaatctgc tcccttactt tgtcatcacc agtctgggaa taagggtatg
                                                                        180
 ccctattcac acctgttaaa agggcgctaa gcatttttga ttcaacatct tttttttga
                                                                        240
 cacaagtccg aaaaaagcaa aagtaaacag ttnttaattt gttagccaat tcactttctt
                                                                        300
 catgggacag agccatttga tttaaaaaagc aaattgcata atattgagct ttgggagctg
                                                                        360
 atatntgage ggaagantag cetttetaet teaceagaea caacteettt catattggga
                                                                        420
 tgttnacnaa agttatgtct cttacagatg ggatgctttt gtggcaattc tg
                                                                        472
       <210> 87
       <211> 413
       <212> DNA
       <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(413)
      <223> n = A,T,C or G
      <400> 87
agaaaccagt atctctnaaa acaacctctc ataccttgtg gacctaattt tgtgtgcgtg
                                                                        60
tgtgtgtgcg cgcatattat atagacaggc acatcttttt tacttttgta aaagcttatg
                                                                        120
cctctttggt atctatatct gtgaaagttt taatgatctg ccataatgtc ttggggacct
                                                                       180
ttgtcttctg tgtaaatggt actagagaaa acacctatnt tatgagtcaa tctagttngt
                                                                       240
tttattcgac atgaaggaaa tttccagatn acaacactna caaactctcc cttgactagg
                                                                       300
ggggacaaag aaaagcanaa ctgaacatna gaaacaattn cctggtgaga aattncataa
                                                                       360
acagaaattg ggtngtatat tgaaananng catcattnaa acgtttttt ttt
                                                                       413
      <210> 88
      <211> 448
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(448)
      <223> n = A, T, C or G
      <400> 88
cgcagcgggt cctctctatc tagctccagc ctctcgcctg ccccactccc cgcgtcccgc
                                                                        60
gtcctagccn accatggccg ggcccctgcg cgccccgctg ctcctgctgg ccatcctggc
                                                                       120
cgtggccctg gccgtgagcc ccgcggccgg ctccagtccc ggcaagccgc cgcgcctggt
                                                                       180
gggaggccca tggaccccgc gtggaagaag aaggtgtgcg gcgtgcactg gactttgccg
                                                                       240
teggenanta caacaaacce geaacnactt ttacenagen egegetgeag gttgtgeege
                                                                       300
cccaancaaa ttgttactng gggtaantaa ttcttggaag ttgaacctgg gccaaacnng
                                                                       360
tttaccagaa ccnagccaat tngaacaatt ncccctccat aacagcccct tttaaaaaagg
                                                                       420
gaancantcc tgntcttttc caaatttt
                                                                       448
     <210> 89
      <211> 463
     <212> DNA
     <213> Homo sapien
     <220>
     <221> misc_feature
```

```
<222> (1)...(463)
       \langle 223 \rangle n = \dot{A}, T, C or G
      <400> 89
gaattttgtg cactggccac tgtgatggaa ccattgggcc aggatgcttt gagtttatca
                                                                          60
gtagtgattc tgccaaagtt ggtgttgtaa catgagtatg taaaatgtca aaaaattagc
                                                                         120
agaggtctag gtctgcatat cagcagacag tttgtccgtg tattttgtag ccttgaagtt
                                                                        180
ctcagtgaca agttnnttct gatgcgaagt tctnattcca gtgttttagt cctttgcatc
                                                                         240
tttnatgttn agacttgcct ctntnaaatt gcttttgtnt tctgcaggta ctatctgtgg
                                                                         300
tttaacaaaa tagaannact tctctgcttn gaanatttga atatcttaca tctnaaaatn
                                                                         360
aattctctcc ccatannaaa acccangccc ttggganaat ttgaaaaang gntccttcnn
                                                                         420
aattonnana anttoagntn toatacaaca naacngganc ccc
                                                                         463
      <210> 90
      <211> 400
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc feature
      <222> (1)...(400)
      \langle 223 \rangle n = A,T,C or G
      <400> 90
agggattgaa ggtctnttnt actgtcggac tgttcancca ccaactctac aagttgctgt
cttccactca ctgtctgtaa gcntnttaac ccagactgta tcttcataaa tagaacaaat
                                                                         120
tcttcaccag tcacatcttc taggaccttt ttggattcag ttagtataag ctcttccact
                                                                         180
tcctttgtta agacttcatc tggtaaagtc ttaagttttg tagaaaggaa tttaattgct
                                                                         240
cgttctctaa caatgtcctc tccttgaagt atttggctga acaacccacc tnaaqtccct
                                                                         300
ttgtgcatcc attttaaata tacttaatag ggcattggtn cactaggtta aattctgcaa
                                                                         360
gagtcatctg tctgcaaaag ttgcgttagt atatctgcca
                                                                         400
      <210> 91
      <211> 480
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(480)
      \langle 223 \rangle n = A,T,C or G
      <400> 91
gageteggat ecaataatet ttgtetgagg geageacaea tatneagtge eatggnaact
                                                                         60
ggtctacccc acatgggagc agcatgccgt agntatataa ggtcattccc tgagtcagac
                                                                        120
atgcctcttt gactaccgtg tgccagtgct ggtgattctc acacacctcc nnccgctctt
                                                                        180
tgtggaaaaa ctggcacttg nctggaacta gcaagacatc acttacaaat tcacccacga
                                                                        240
gacacttgaa aggtgtaaca aagcgactct tgcattgctt tttgtccctc cggcaccagt
                                                                        300
tgtcaatact aaccegetgg tttgcctcca tcacatttgt gatetgtage tetggataca
                                                                        360
tetectgaca gtactgaaga acttettett ttgttteaaa ageaactett ggtgeetgtt
                                                                        420
ngatcaggtt cccatttccc agtccgaatg ttcacatggc atainttact tcccacaaaa
                                                                        480
```

<210> 92

<211> 477

<212> DNA

```
<213> Homo sapien
        <220>
        <221> misc_feature
        <222> (1)...(477)
        <223> n = A, T, C \text{ or } G
       <400> 92
 atacagecca nateccaeca egaagatgeg ettgttgaet gagaacetga tgeggteaet
                                                                         60
 ggtcccgctg tagccccagc gactetccac ctgctggaag cggttgatgc tgcactcctt
                                                                         120
 cccacgcagg cagcagcggg gccggtcaat gaactccact cgtggcttgg ggttgacggt
                                                                         180
 taantgcagg aagaggctga ccacctcgcg gtccaccagg atgcccgact gtgcgggacc
                                                                         240
 tgcagcgaaa ctcctcgatg gtcatgagcg ggaagcgaat gangcccagg gccttgccca
                                                                         300
 gaacetteeg cetgttetet ggegteacet geagetgetg cegetnacae teggeetegg
                                                                         360
 accageggae aaaeggegtt gaacageege aceteaegga tgeecantgt gtegegetee
                                                                         420
 aggaacggcn ccagcgtgtc caggtcaatg tcggtgaanc ctccgcgggt aatggcg
                                                                         477
       <210> 93
       <211> 377
       <212> DNA
      <213> Homo sapien
       <220>
       <221> misc_feature
       <222> (1)...(377)
       <223> n = A,T,C or G
       <400> 93
gaacggctgg accttgcctc gcattgtgct gctggcagga ataccttggc aagcagctcc
                                                                         60.
agtecgagea geeccagace getgeegeec gaagetaage etgeetetgg cetteceete
                                                                        120
cgcctcaatg cagaaccant agtgggagca ctgtgtttag agttaagagt gaacactgtn
                                                                        180
tgattttact tgggaatttc ctctgttata tagcttttcc caatgctaat ttccaaacaa
caacaacaaa ataacatgtt tgcctgttna gttgtataaa agtangtgat tctgtatnta
                                                                        300
aagaaaatat tactgttaca tatactgctt gcaanttctg tatttattgg tnctctggaa
                                                                       360
ataaatatat tattaaa
                                                                        377
      <210> 94
     <211> 495
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(495)
      \langle 223 \rangle n = A,T,C or G
      <400> 94
ccctttgagg ggttagggtc cagttcccag tggaagaaac aggccaggag aantgcgtgc
                                                                        60
cgagctgang cagatttecc acagtgaccc cagageeetg ggetatagte tetgaccet
                                                                       120
ccaaggaaag accaccttct ggggacatgg gctggagggc aggacctaga ggcaccaagg
                                                                       180
gaaggcccca ttccggggct gttccccgag gaggaaggga aggggctctg tgtgccccc
                                                                       240
acgaggaana ggccctgant cctgggatca nacacccctt cacgtgtatc cccacacaaa
                                                                       300
tgcaagctca ccaaggtccc ctctcagtcc cttccctaca ccctgaacgg ncactggccc
                                                                       360
acacccaccc agancancca cccgccatgg ggaatgtnct caaggaatcg cngggcaacg
                                                                       420
tggactctng tcccnnaagg gggcagaatc tccaatagan gganngaacc cttgctnana
```

```
aaaaaaana aaaaa
                                                                       495
       <210> 95
       <211> 472
       <212> DNA
       <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(472)
      <223> n = A,T,C or G
      <400> 95
ggttacttgg tttcattgcc accacttagt ggatgtcatt tagaaccatt ttgtctgctc
                                                                        60
cctctggaag ccttgcgcag agcggacttt gtaattgttg gagaataact gctgaatttt
                                                                       120
tagctgtttt gagttgattc gcaccactgc accacaactc aatatgaaaa ctatttnact
                                                                       180
tatttattat cttgtgaaaa gtatacaatg aaaattttgt tcatactgta tttatcaagt
                                                                       240
atgatgaaaa gcaatagata tatattettt tattatgttn aattatgatt gccattatta
                                                                       300
ateggeaaaa tgtggagtgt atgttetttt cacagtaata tatgeetttt gtaaetteae
                                                                       360
ttggttattt tattgtaaat gaattacaaa attcttaatt taagaaaatg gtangttata
                                                                       420
tttanttcan taatttcttt ccttgtttac gttaattttg aaaagaatgc at
      <210> 96
      <211> 476
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(476)
      <223> n = A,T,C or G
      <400> 96
ctgaagcatt tcttcaaact tntctacttt tgtcattgat acctgtagta agttgacaat
                                                                       60
gtggtgaaat ttcaaaatta tatgtaactt ctactagttt tactttctcc cccaagtctt
                                                                      120
ttttaactca tgatttttac acacacaatc cagaacttat tatatagcct ctaagtcttt
                                                                      180
attetteaca gtagatgatg aaagagteet ccagtgtett gngcanaatg ttetagntat
                                                                      240
agctggatac atacngtggg agttctataa actcatacct cagtgggact naaccaaaat
                                                                      300
tgtgttagtc tcaattccta ccacactgag ggagcctccc aaatcactat attcttatct
                                                                      360
gcaggtactc ctccagaaaa acngacaggg caggcttgca tgaaaaagtn acatctgcgt
                                                                      420
tacaaagtct atcttcctca nangtctgtn aaggaacaat ttaatcttct agcttt
                                                                      476
      <210> 97
      <211> 479
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1) ... (479)
      <223> n = A,T,C or G
      <400> 97
actctttcta atgctgatat gatcttgagt ataagaatgc atatgtcact agaatggata
                                                                       60
aaataatgct gcaaacttaa tgttcttatg caaaatggaa cgctaatgaa acacagctta
```

```
caatcgcaaa tcaaaactca caagtgctca tctgttgtag atttagtgta ataagactta
                                                                           180
    gattgtgctc cttcggatat gattgtttct canatcttgg gcaatnttcc ttagtcaaat
                                                                           240
    caggctacta gaattctgtt attggatatn tgagagcatg aaatttttaa naatacactt
                                                                           300
    gtgattatna aattaatcac aaatttcact tatacctgct atcagcagct agaaaaacat
                                                                           360
   ntnnttttta natcaaagta ttttgtgttt ggaantgtnn aaatgaaatc tgaatgtggg
                                                                           420
    ttcnatctta ttttttcccn gacnactant tnctttttta gggnctattc tganccatc
                                                                           479
         <210> 98
         <211> 461
         <212> DNA
         <213> Homo sapien
         <400> 98
   agtgacttgt cctccaacaa aaccccttga tcaagtttgt ggcactgaca atcagaccta
                                                                           60
   tgctagttcc tgtcatctat tcgctactaa atgcagactg gaggggacca aaaaggggca
                                                                          120
   tcaactccag ctggattatt ttggagcctg caaatctatt cctacttgta cggactttga
                                                                          180
agtgattcag tttcctctac ggatgagaga ctggctcaag aatatcctca tgcagcttta
                                                                          240
   tgaagccact ctgaacacgc tggttatcta gatgagaaca gagaaataaa gtcagaaaat
                                                                          300
   ttacctggag aaaagaggct ttggctgggg accatcccat tgaaccttct cttaaggact
                                                                          360
   ttaagaaaaa ctaccacatg ttgtgtatcc tggtgccggc cgtttatgaa ctgaccaccc
                                                                          420
   tttggaataa tcttgacgct cctgaacttg ctcctctgcg a
                                                                          461
         <210> 99
         <211> 171
         <212> DNA
         <213> Homo sapien
         <400> 99
   gtggccgcgc gcaggtgttt cctcgtaccg cagggccccc tcccttcccc aggcgtccct
                                                                           60
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tagcggggtg	aatattttat	actotaacto	agraatrara	acaacytcyt atataatat	tetacteses	3240
	ctttcttata					3300
	aaaaaaaaaa				aaaaaaaaaa	3360
~~~~~~~	uuddaddadd,	aaaaaaaaa	aaaaadatad	aaaaaddddd	,	3410

<sup>&</sup>lt;210> 111

<sup>&</sup>lt;211> 1289

<sup>&</sup>lt;212> DNA

<sup>&</sup>lt;213> Homo sapien

## <400> 111

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<210> 112

<211> 315

<212> PRT

<213> Homo sapien

## <400> 112

Met Val Phe Thr Val Arg Leu Leu His Ile Phe Thr Val Asn Lys Gln - 5 10 Leu Gly Pro Lys Ile Val Ile Val Ser Lys Met Met Lys Asp Val Phe 20 25 30 Phe Phe Leu Phe Phe Leu Gly Val Trp Leu Val Ala Tyr Gly Val Ala 35 -40 45 Thr Glu Gly Leu Leu Arg Pro Arg Asp Ser Asp Phe Pro Ser Ile Leu - 55 60 Arg Arg Val Phe Tyr Arg Pro Tyr Leu Gln Ile Phe Gly Gln Ile Pro 70 75 Gln Glu Asp Met Asp Val Ala Leu Met Glu His Ser Asn Cys Ser Ser 85 90 Glu Pro Gly Phe Trp Ala His Pro Pro Gly Ala Gln Ala Gly Thr Cys 100 -105 110 Val Ser Gln Tyr Ala Asn Trp Leu Val Val Leu Leu Val Ile Phe 120 Leu Leu Val Ala Asn Ile Leu Leu Val Asn Leu Leu Ile Ala Met Phe 135 140 Ser Tyr Thr Phe Gly Lys Val Gln Gly Asn Ser Asp Leu Tyr Trp Lys 145 150 155 Ala Gln Arg Tyr Arg Leu Ile Arg Glu Phe His Ser Arg Pro Ala Leu 165 170 175 Ala Pro Pro Phe Ile Val Ile Ser His Leu Arg Leu Leu Leu Arg Gln 185 Leu Cys Arg Arg Pro Arg Ser Pro Gln Pro Ser Ser Pro Ala Leu Glu

195 200 His Phe Arg Val Tyr Leu Ser Lys Glu Ala Glu Arg Lys Leu Leu Thr 215 220 Trp Glu Ser Val His Lys Glu Asn Phe Leu Leu Ala Arg Ala Arg Asp 230 235 Lys Arg Glu Ser Asp Ser Glu Arg Leu Lys Arg Thr Ser Gln Lys Val 245 250 Asp Leu Ala Leu Lys Gln Leu Gly His Ile Arg Glu Tyr Glu Gln Arg Leu Lys Val Leu Glu Arg Glu Val Gln Gln Cys Ser Arg Val Leu Gly 280 Trp Val Ala Glu Ala Leu Ser Arg Ser Ala Leu Leu Pro Pro Gly Gly 295 Pro Pro Pro Pro Asp Leu Pro Gly Ser Lys Asp 310

<210> 113 <211> 553 <212> PRT

<213> Homo sapien

<400> 113

Met Val Gln Arg Leu Trp Val Ser Arg Leu Leu Arg His Arg Lys Ala - 10 Gln Leu Leu Val Asn Leu Leu Thr Phe Gly Leu Glu Val Cys Leu 25 Ala Ala Gly Ile Thr Tyr Val Pro Pro Leu Leu Glu Val Gly Val 40 Glu Glu Lys Phe Met Thr Met Val Leu Gly Ile Gly Pro Val Leu Gly 55 Leu Val Cys Val Pro Leu Leu Gly Ser Ala Ser Asp His Trp Arg Gly 75 Arg Tyr Gly Arg Arg Pro Phe Ile Trp Ala Leu Ser Leu Gly Ile 85 90 Leu Leu Ser Leu Phe Leu Ile Pro Arg Ala Gly Trp Leu Ala Gly Leu 105 . Leu Cys Pro Asp Pro Arg Pro Leu Glu Leu Ala Leu Leu Ile Leu Gly 120 125 Val Gly Leu Leu Asp Phe Cys Gly Gln Val Cys Phe Thr Pro Leu Glu 135 Ala Leu Leu Ser Asp Leu Phe Arg Asp Pro Asp His Cys Arg Gln Ala 150 155 Tyr Ser Val Tyr Ala Phe Met Ile Ser Leu Gly Gly Cys Leu Gly Tyr 170 Leu Leu Pro Ala Ile Asp Trp Asp Thr Ser Ala Leu Ala Pro Tyr Leu 185 Gly Thr Gln Glu Cys Leu Phe Gly Leu Leu Thr Leu Ile Phe Leu 200 -Thr Cys Val Ala Ala Thr Leu Leu Val Ala Glu Glu Ala Ala Leu Gly 215 220 Pro Thr Glu Pro Ala Glu Gly Leu Ser Ala Pro Ser Leu Ser Pro His 230 235 Cys Cys Pro Cys Arg Ala Arg Leu Ala Phe Arg Asn Leu Gly Ala Leu 250 Leu Pro Arg Leu His Gln Leu Cys Cys Arg Met Pro Arg Thr Leu Arg

265 Arg Leu Phe Val Ala Glu Leu Cys Ser Trp Met Ala Leu Met Thr Phe 280 Thr Leu Phe Tyr Thr Asp Phe Val Gly Glu Gly Leu Tyr Gln Gly Val 295 Pro Arg Ala Glu Pro Gly Thr Glu Ala Arg Arg His Tyr Asp Glu Gly 310 315 Val Arg Met Gly Ser Leu Gly Leu Phe Leu Gln Cys Ala Ile Ser Leu 330 Val Phe Ser Leu Val Met Asp Arg Leu Val Gln Arg Phe Gly Thr Arg 340 345 Ala Val Tyr Leu Ala Ser Val Ala Ala Phe Pro Val Ala Ala Gly Ala 360 Thr Cys Leu Ser His Ser Val Ala Val Val Thr Ala Ser Ala Ala Leu 375 380 Thr Gly Phe Thr Phe Ser Ala Leu Gln Ile Leu Pro Tyr Thr Leu Ala 390 395 Ser Leu Tyr His Arg Glu Lys Gln Val Phe Leu Pro Lys Tyr Arg Gly 405 410 Asp Thr Gly Gly Ala Ser Ser Glu Asp Ser Leu Met Thr Ser Phe Leu 425 Pro Gly Pro Lys Pro Gly Ala Pro Phe Pro Asn Gly His Val Gly Ala 440 Gly Gly Ser Gly Leu Leu Pro Pro Pro Pro Ala Leu Cys Gly Ala Ser 455 Ala Cys Asp Val Ser Val Arg Val Val Val Gly Glu Pro Thr Glu Ala 470 . 475 Arg Val Val Pro Gly Arg Gly Ile Cys Leu Asp Leu Ala Ile Leu Asp .485 490 495 Ser Ala Phe Leu Leu Ser Gln Val Ala Pro Ser Leu Phe Met Gly Ser 505 Ile Val Gln Leu Ser Gln Ser Val Thr Ala Tyr Met Val Ser Ala Ala 520 525 Gly Leu Gly Leu Val Ala Ile Tyr Phe Ala Thr Gln Val Val Phe Asp 535 Lys Ser Asp Leu Ala Lys Tyr Ser Ala 550

<210> 114

<211> 241

<212> PRT

<213> Homo sapien

<400> 114

 Met
 Gln
 Cys
 Phe
 Ser
 Phe
 Ile
 Lys
 Thr
 Met
 Met
 Ile
 Leu
 Phe
 Asn
 Leu

 1
 5
 5
 10
 10
 11
 15
 15

 Leu
 Ile
 Phe
 Leu
 Cys
 Gly
 Ala
 Ala
 Ala
 Leu
 Leu
 Ala
 Val
 Ile
 Ala
 Ile
 Ala
 Ile
 Phe
 Ile
 Ile
 Ala
 Ile
 Ala
 Ile
 Ile
 Ile
 I

				85					90					95	-		
Phe	Ile	Ala		Val	Ala	Ala	Ala		Val	Ala	Leu	Val	Tyr	Thr	Thr		
			100		_		_	105	_ · _			_	110				
Met	Ala		His	Phe	Leu	Thr		Leu	Val	Val	Pro		Ile	Lys	Lys	•	
3	m	115	C	a1-	<b>a</b> 2	3	120	6713a aa	<b>~</b> 12 ~	**- 7	<b></b>	125	_			•	
Asp	131	GIY	Ser	Gin	GIU	135	Pne	inr.	GIN	vaı	_	Asn	Thr	Thr	Met		
Tare		T.AU	Tare	Cva	Cva		Dha	Thr	λan	Tree	140	A con	Bho	Glu	3		·
145	Gry	neu	цуз	Cys	150		FIIC	1111	ASII	155	1111	wsh	FILE	GIU	160		
	Pro	Tvr	Phe	Lvs			Ser	Ala	Phe		Pro	Phe	Cva	Cys			
		-4		165					170				0,0	175			
Asp	Asn	Val	Thr	Asn	Thr	Ala	Asn	Glu	Thr	Cys	Thr	Lys	Gln	Lys	Ala		
_			180					185				•	190	-			
His	Asp	Gln	Lys	Val	Glu	Gly	Cys	Phe	Asn	Gln	Leu	Leu	Tyr	Asp	Ile		
	•	195		•			200		•			205				:	:·.
Arg		Asn	Ala	Val	Thr		Gly	Gly	Val	Ala	Ala	Gly	Ile	Gly	Gly		
	210					215					220						•
	Glu	Leu	Ala	Ala			Val	Ser	Met		Leu	Tyr	Cys	Asn	Leu		
225					230					235				•	240		:
Gln						•			•						<b>—</b>		
					•										•		
	<2	210>	115							•				•			
		211>									•	٠.			•	•	•
	<2	212>	DNA						• •								
	<2	213>	Homo	sap	oien									·			
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		00>															
gctc	tttc	tc t	:cccc	tcct	c tg	aatt	taat	tct	ttca	act	tgca	attt	gc a	aagga	ttaca		60
															attac		120
															tctga		180
															atggt tgggt		240
															.cgggc :gaagt		300 360
ttag		.09 0				.cgcc			9000	Cut	adaa	gccc	yr :	Jacki	.yaayt	•	366
	,																300
•	<2	10>	116									•					
	<2	11>	282										•			•	
	<2	12>	DNA														
	<2	13>	Homo	sap	ien						٠			٠,			٠.
		20>		_		•											
			misc			:								•			
			(1).									•	:		•		
	<2	25>	n =	А,Т,	c or	G											•
	_A	۸۸-	116														
acaa.		00>		ttee	+ =+	atte	tago	222	atte	222	tata	~~~	+ - 4	. + _ + _	atatt		<b>C</b> 0
															ctcaa		60
															ggttc		120 180
															tatgt		240
			ctat									3304	·		-ucyt		282
		_							_								

<210> 117

<211> 305

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<212> DNA
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       <220>
       <221> misc_feature
       <222> (1)...(305)
       <223> n = A,T,C or G
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                                                                           60.
tatttateet eeeteetgaa acaattgeaa aataanacaa aatatatgaa acaattgeaa
                                                                          120
aataaggcaa aatatatgaa acaacaggtc tcgagatatt ggaaatcagt caatgaagga
                                                                          180
tactgatccc tgatcactgt cctaatgcag gatgtgggaa acagatgagg tcacctctgt
                                                                          240
gactgcccca gcttactgcc tgtagagagt ttctangctg cagttcagac agggagaaat
                                                                          300
tgggt
                                                                          305
       <210> 118
       <211> 71
       <212> DNA
       <213> Homo sapien
       <220>
       <221> misc feature
       <222> (1)...(71)
       \langle 223 \rangle n = A,T,C or G
      <400> 118
accaaggtgt ntgaatetet gacgtgggga tetetgatte eegcacaate tgagtggaaa
                                                                          60
aantcctggg t
      <210> 119
      <211> 212
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1) ... (212)
      <223> n = A,T,C or G
      <400> 119
actccggttg gtgtcagcag cacgtggcat tgaacatngc aatgtggagc ccaaaccaca
                                                                         60
gaaaatgggg tgaaattggc caactttcta tnaacttatg ttggcaantt tgccaccaac
                                                                         120
agtaagctgg cccttctaat aaaagaaaat tgaaaggttt ctcactaanc ggaattaant
                                                                         180
aatggantca aganactccc aggcctcagc gt
                                                                         212
      <210> 120
      <211> 90
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(90)
     <223> n = A, T, C or G
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<400> 120	
actcgttgca natcaggggc cccccagagt cacc	gttgca ggagtccttc tggtcttgcc 60
ctccgccggc gcagaacatg ctggggtggt	90
	. ,
<210> 121	
<211> 218	and the second s
<212> DNA	
<213> Homo sapien	
<213> Homo Sapten	
<220>	
·	
<221> misc_feature	
<222> (1) (218)	
$\langle 223 \rangle$ n = A,T,C or G	
<400> 121	
tgtancgtga anacgacaga nagggttgtc aaaa	atggag aancettgaa gteattttga 60
gaataagatt tgctaaaaga tttggggcta aaac	atggtt attgggagac atttctgaag 120
atatncangt aaattangga atgaattcat ggtt	cttttg ggaattcctt tacgatngcc 180
agcatanact tcatgtgggg atancagcta ccct	tgta 218
<210> 122	
<211> 171	
<212> DNA	
<213> Homo sapien	
•	
<400> 122	
taggggtgta tgcaactgta aggacaaaaa ttga	gactca actggcttaa ccaataaagg 60
catttgttag ctcatggaac aggaagtcgg atgg	tggggc atcttcagtg ctgcatgagt 120
caccacccg gcggggtcat ctgtgccaca ggtc	
	J J
<210> 123	
<211> 76	
<212> DNA	
<213> Homo sapien	
<220>	
<221> misc_feature	
<222> (1) (76)	-
$\langle 223 \rangle$ n = A,T,C or G	
(2237 H = A,1,0 OL 6	
<400> 123	
tgtagcgtga agacnacaga atggtgtgtg ctgtg	
ttatcaanta ttgtgt	76
-210. 104	
<210> 124	
<211> 131	•
<212> DNA	
<213> Homo sapien	
<400> 124	
acctttcccc aaggccaatg tcctgtgtgc taact	ggccg gctgcaggac agctgcaatt 60
caatgtgctg ggtcatatgg aggggaggag actct	aaaat agccaatttt attctcttgg 120
ttaagatttg t	131

```
<210> 125
       <211> 432
       <212> DNA
       <213> Homo sapien
       <400> 125
actttatcta ctggctatga aatagatggt ggaaaattgc gttaccaact ataccactgg
                                                                         60
cttgaaaaag aggtgatagc tcttcagagg acttgtgact tttgctcaga tgctgaagaa
                                                                        120
ctacagtctg catttggcag aaatgaagat gaatttggat taaatgagga tgctgaagat
                                                                        180
ttgcctcacc aaacaaagt gaaacaactg agagaaaatt ttcaggaaaa aagacagtgg
                                                                        240
ctcttgaagt atcagtcact tttgagaatg tttcttagtt actgcatact tcatggatcc
                                                                        300
catggtgggg gtcttgcatc tgtaagaatg gaattgattt tgcttttgca agaatctcag
                                                                        360
caggaaacat cagaaccact attttctagc cctctgtcag agcaaacctc agtgcctctc
                                                                        420
ctctttgctt gt
                                                                        432
      <210> 126
      <211> 112
      <212> DNA
      <213> Homo sapien
      <400> 126
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                                                                         60
agtaagaatg atatttcccc ccagggatca ccaaatattt ataaaaattt gt
                                                                        112
      <210> 127
      <211> 54
      <212> DNA
      <213> Homo sapien
      <400> 127
accacgaaac cacaaacaag atggaagcat caatccactt gccaagcaca gcag
                                                                         54
      <210> 128
      <211> 323
      <212> DNA
      <213> Homo sapien
      <400> 128
acctcattag taattgtttt gttgtttcat ttttttctaa tgtctccct ctaccagetc
                                                                        60
acctgagata acagaatgaa aatggaagga cagccagatt teteetttge tetetgetca
                                                                       120
ttctctctga agtctaggtt acccattttg gggacccatt ataggcaata aacacagttc
                                                                        180
ccaaagcatt tggacagttt cttgttgtgt tttagaatgg ttttcctttt tcttagcctt
                                                                       240
ttcctgcaaa aggctcactc agtcccttgc ttgctcagtg gactgggctc cccagggcct
                                                                       300
aggctgcctt cttttccatg tcc
                                                                       323
      <210> 129
      <211> 192
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
     <222> (1)...(192)
      \langle 223 \rangle n = A,T,C or G
```

```
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                                                                         60
tgaaaacaca ctaacataat ttntgtgaac catgatcaga tacaacccaa atcattcatc
                                                                         120
tagcacattc atctgtgata naaagatagg tgagtttcat ttccttcacg ttggccaatg
                                                                         180
gataaacaaa gt
                                                                         192
      <210> 130
       <211> 362
       <212> DNA
       <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(362)
      <223> n = A,T,C or G
      <400> 130
ccctttttta tggaatgagt agactgtatg tttgaanatt tanccacaac ctctttgaca
                                                                         60
tataatgacg caacaaaaag gtgctgttta gtcctatggt tcagtttatg cccctgacaa
                                                                        120
gtttccattg tgttttgccg atcttctggc taatcgtggt atcctccatg ttattagtaa
                                                                        180
ttctgtattc cattttgtta acgcctggta gatgtaacct gctangaggc taactttata
                                                                        240
cttatttaaa agctcttatt ttgtggtcat taaaatggca atttatgtgc agcactttat
                                                                        300
tgcagcagga agcacgtgtg ggttggttgt aaagctcttt gctaatctta aaaagtaatg
                                                                        360
gg
                                                                        362
      <210> 131
      <211> 332
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(332)
      <223> n = A,T,C or G
      <400> 131
ctttttgaaa gatcgtgtcc actcctgtgg acatcttgtt ttaatggagt ttcccatgca
                                                                         60
gtangactgg tatggttgca gctgtccaga taaaaacatt tgaagagctc caaaatgaga
                                                                       120
gttctcccag gttcgccctg ctgctccaag tctcagcagc agcctctttt aggaggcatc
                                                                        180
ttctgaacta gattaaggca gcttgtaaat ctgatgtgat ttggtttatt atccaactaa
                                                                        240
cttccatctg ttatcactgg agaaagccca gactccccan gacnggtacg gattgtgggc
                                                                        300
atanaaggat tgggtgaagc tggcgttgtg gt
                                                                        332
      <210> 132
      <211> 322
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(322)
      \langle 223 \rangle n = A,T,C or G
      <400> 132
```

```
agtggctaag agaactcgat ttcaagcaat tctgaaagga aaaccagcat gacacagaat
                                                                         120
 ctcaaattcc caaacagggg ctctgtggga aaaatgaggg aggacctttg tatctcgggt
                                                                         180
 tttagcaagt taaaatgaan atgacaggaa aggcttattt atcaacaaag agaagagttg
                                                                         240
 ggatgcttct aaaaaaaact ttggtagaga aaataggaat gctnaatcct agggaagcct
                                                                         300
 gtaacaatct acaattggtc ca
                                                                         322
       <210> 133
      <211> 278
       <212> DNA
       <213> Homo sapien
       <220>
       <221> misc_feature
       <222> (1)...(278)
       \langle 223 \rangle n = A,T,C or G
    ··· <400> 133
acaagcotto acaagtttaa ctaaattggg attaatottt ctgtanttat ctgcataatt
                                                                         60
cttgtttttc tttccatctg gctcctgggt tgacaatttg tggaaacaac tctattgcta
                                                                         120
ctatttaaaa aaaatcacaa atctttccct ttaagctatg ttnaattcaa actattcctg
                                                                         180
ctattcctgt tttgtcaaag aaattatatt tttcaaaata tgtntatttg tttgatgggt
                                                                         240
cccacgaaac actaataaaa accacagaga ccagcctg
                                                                        278
      <210> 134
      <211> 121
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(121)
      <223> n = A,T,C or G
      <400> 134
gtttanaaaa cttgtttagc tccatagagg aaagaatgtt aaactttgta ttttaaaaca
                                                                         60
tgattctctg aggttaaact tggttttcaa atgttatttt tacttgtatt ttgcttttgg
                                                                        120
                                                                        121
      <210> 135
      <211> 350
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(350)
      <223> n = A,T,C or G
      <400> 135
acttanaacc atgectagea cateagaate ceteaaagaa cateagtata ateetatace
                                                                         60
atancaagtg gtgactggtt aagcgtgcga caaaggtcag ctggcacatt acttgtgtgc
                                                                        120
aaacttgata cttttgttct aagtaggaac tagtatacag tncctaggan tggtactcca
                                                                       180
gggtgccccc caactcctgc agccgctcct ctgtgccagn ccctgnaagg aactttcgct
                                                                       240
ccacctcaat caagecetgg gecatgetae etgeaattgg etgaacaaac gtttgetgag
                                                                       300
ttcccaagga tgcaaagcct ggtgctcaac tcctggggcg tcaactcagt
                                                                       350
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<211> 382

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<210> 136
      <211> 399
       <212> DNA
       <213> Homo sapien
       <220>
       <221> misc_feature
       <222> (1)...(399)
       \langle 223 \rangle n = A,T,C or G
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                                                                          60
gctgtgattg tatccgaata ntcctcgtga gaaaagataa tgagatgacg tgagcagcct
                                                                         120
gcagacttgt gtctgccttc aanaagccag acaggaaggc cctgcctgcc ttggctctga
                                                                         180
cctggcggcc agccagccag ccacaggtgg gcttcttcct tttgtggtga caacnccaag
                                                                         240
aaaactgcag aggcccaggg tcaggtgtna gtgggtangt gaccataaaa caccaggtgc
                                                                         300
teccaggaac eegggeaaag gecateeeca eetacageea geatgeecae tggegtgatg
                                                                         360
ggtgcagang gatgaagcag ccagntgttc tgctgtggt
                                                                         399
      <210> 137
      <211> 165
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1) ... (165)
      <223> n = A,T,C or G
      <400> 137
actggtgtgg tngggggtga tgctggtggt anaagttgan gtgacttcan gatggtgtgt
                                                                         60
ggaggaagtg tgtgaacgta gggatgtaga ngttttggcc gtgctaaatg agcttcggga
                                                                         120
ttggctggtc ccactggtgg tcactgtcat tggtggggtt cctgt
      <210> 138
      <211> 338
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1) ... (338)
      \langle 223 \rangle n = A,T,C or G
      <400> 138
actcactgga atgccacatt cacaacagaa tcagaggtct gtgaaaacat taatggctcc
                                                                         60
ttaacttctc cagtaagaat cagggacttg aaatggaaac gttaacagcc acatgcccaa
                                                                        120
tgctgggcag tctcccatgc cttccacagt gaaagggctt gagaaaaatc acatccaatg
                                                                        180
tcatgtgttt ccagccacac caaaaggtgc ttggggtgga gggctggggg catananggt
                                                                        240
cangecteag gaageeteaa gtteeattea getttgeeae tgtacattee eeatntttaa
                                                                        300
aaaaactgat gcctttttt tttttttttg taaaattc
      <210> 139
```

```
<212> DNA
       <213> Homo sapien
       <400> 139
 gggaatcttg gtttttggca tctggtttgc ctatagccga ggccactttg acagaacaaa
                                                                          60
 gaaagggact tcgagtaaga aggtgattta cagccagcct agtgcccgaa gtgaaggaga
                                                                         120
 atteaaacag acctegteat teetggtgtg ageetggteg geteacegee tateatetge
                                                                         180
atttgcctta ctcaggtgct accggactct ggcccctgat gtctgtagtt tcacaggatg
                                                                         240
ccttatttgt cttctacacc ccacagggcc ccctacttct tcggatgtgt ttttaataat
                                                                         300
gtcagctatg tgccccatcc tccttcatgc cctccctccc tttcctacca ctgctgagtg
                                                                         360
gcctggaact tgtttaaagt gt
                                                                         382
       <210> 140
      <211> 200
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(200)
      <223> n = A,T,C or G
      <400> 140
accaaanctt ctttctgttg tgttngattt tactataggg gtttngcttn ttctaaanat
                                                                         .60
actiticati taacanciii tgitaagigi caggeigeae tiigeteeat anaattatig
                                                                        120
ttttcacatt tcaacttgta tgtgtttgtc tcttanagca ttggtgaaat cacatatttt
                                                                        180
atattcagca taaaggagaa
                                                                        200
      <210> 141
      <211> 335
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1) ... (335)
      <223> n = A,T,C or G
      <400> 141
actttatttt caaaacactc atatgttgca aaaaacacat agaaaaataa agtttggtgg
                                                                        60
gggtgctgac taaacttcaa gtcacagact tttatgtgac agattggagc agggtttgtt
atgcatgtag agaacccaaa ctaatttatt aaacaggata gaaacaggct gtctgggtga
                                                                        180
aatggttctg agaaccatcc aattcacctg tcagatgctg atanactagc tcttcagatg
                                                                        240
tttttctacc agttcagaga tnggttaatg actanttcca atggggaaaa agcaagatgg
                                                                        300
attcacaaac caagtaattt taaacaaaga cactt
                                                                        335
      <210> 142
      <211> 459
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(459)
     \langle 223 \rangle n = A,T,C or G
```

```
<400> 142
accaggitaa tattgccaca tatatccttt ccaattgcgg gctaaacaga cgtgtattta
                                                                         60
gggttgttta aagacaaccc agcttaatat caagagaaat tgtgaccttt catggagtat
                                                                        120
ctgatggaga aaacactgag ttttgacaaa tcttatttta ttcagatagc agtctgatca
                                                                        180
cacatggtcc aacaacactc aaataataaa tcaaatatna tcagatgtta aagattggtc
                                                                        240
ttcaaacatc atagccaatg atgccccgct tgcctataat ctctccgaca taaaaccaca
                                                                        300
tcaacacctc agtggccacc aaaccattca gcacagcttc cttaactgtg agctgtttga
                                                                        360
agctaccagt ctgagcacta ttgactatnt ttttcangct ctgaatagct ctagggatct
                                                                        420
cagcangggt gggaggaacc agctcaacct tggcgtant
                                                                        459
      <210> 143
      <211> 140
       <212> DNA
      <213> Homo sapien
      <400> 143
acattteett ecaecaagte aggacteetg gettetgtgg gagttettat cacetgaggg
aaatccaaac agtctctcct agaaaggaat agtgtcacca accccaccca tctccctgag
                                                                        120
accatccgac ttccctgtgt
                                                                        140
      <210> 144
      <211> 164
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(164)
      <223> n = A,T,C or G
      <400> 144
acttcagtaa caacatacaa taacaacatt aagtgtatat tgccatcttt gtcattttct
                                                                        . 60
atctatacca ctctcccttc tgaaaacaan aatcactanc caatcactta tacaaatttg
                                                                        120
aggcaattaa tccatatttg ttttcaataa ggaaaaaaag atgt
                                                                       164
      <210> 145
      <211> 303
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(303)
      \langle 223 \rangle n = A,T,C or G
      <400> 145
acgtagacca tccaactttg tatttgtaat ggcaaacatc cagnagcaat tcctaaacaa
                                                                        60
actggagggt atttataccc aattatccca ttcattaaca tgccctcctc ctcaggctat
                                                                       120
gcaggacagc tatcataagt cggcccaggc atccagatac taccatttgt ataaacttca
                                                                       180
gtaggggagt ccatccaagt gacaggtcta atcaaaggag gaaatggaac ataagcccag
                                                                       240
tagtaaaatn ttgcttagct gaaacagcca caaaagactt accgccgtgg tgattaccat
                                                                       300
caa
                                                                       303
```

```
<211> 327
        <212> DNA
        <213> Homo sapien
        <220>
        <221> misc_feature
        <222> (1) ... (327)
        <223> n = A,T,C or G
       <400> 146
 actgcagctc aattagaagt ggtctctgac tttcatcanc ttctccctgg gctccatgac
                                                                         60
 actggcctgg agtgactcat tgctctggtt ggttgagaga gctcctttgc caacaggcct
                                                                         120
 ccaagtcagg gctgggattt gtttcctttc cacattctag caacaatatg ctggccactt
                                                                         180
 cctgaacagg gagggtggga ggagccagca tggaacaagc tgccactttc taaagtagcc
                                                                        240
 agacttgccc ctgggcctgt cacacctact gatgaccttc tgtgcctgca ggatggaatg
                                                                        300
 taggggtgag ctgtgtgact ctatggt
                                                                        327
       <210> 147
      <211> 173
       <212> DNA
       <213> Homo sapien
       <220>
       <221> misc_feature
       <222> (1) ... (173)
       <223> n = A,T,C or G
       <400> 147
acattgtttt tttgagataa agcattgana gagctctcct taacgtgaca caatggaagg
                                                                         60
actggaacac atacccacat ctttgttctg agggataatt ttctgataaa gtcttgctgt
                                                                        120
atattcaagc acatatgtta tatattattc agttccatgt ttatagccta gtt
                                                                        173
      <210> 148
      <211> 477
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(477)
      <223> n = A,T,C or G
      <400> 148
acaaccactt tatctcatcg aatttttaac ccaaactcac tcactgtgcc tttctatcct
                                                                        60
atgggatata ttatttgatg ctccatttca tcacacatat atgaataata cactcatact
                                                                       120
gecetactae etgetgeaat aateacatte cetteetgte etgaceetga agecattggg
                                                                       180
gtggtcctag tggccatcag tccangcctg caccttgagc ccttgagctc cattgctcac
                                                                       240
nccancecae etcacegace ceatectett acacagetae etcettgete tetaacecca
                                                                       300
tagattatnt ccaaattcag tcaattaagt tactattaac actctacccg acatgtccag
                                                                       360
caccactggt aagcettete cageeaacae acacacaca acacneacae acacacatat
                                                                       420
ccaggcacag gctacctcat cttcacaatc acccctttaa ttaccatgct atggtgg
                                                                       477
     <210> 149
     <211> 207
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<212> DNA

## <213> Homo sapien <400> 149 acagttgtat tataatatca agaaataaac ttgcaatgag agcatttaag agggaagaac 60 taacgtattt tagagagcca aggaaggttt ctgtggggag tgggatgtaa ggtggggcct 120 gatgataaat aagagtcagc caggtaagtg ggtggtgtgg tatgggcaca gtgaagaaca 180 tttcaggcag agggaacagc agtgaaa 207 <210> 150 <211> 111 <212> DNA <213> Homo sapien <220> <221> misc\_feature <222> (1) ... (111) <223> n = A,T,C or G<400> 150 accttgattt cattgctgct ctgatggaaa cccaactatc taatttagct aaaacatggg cacttaaatg tggtcagtgt ttggacttgt taactantgg catctttggg t 111 <210> 151 <211> 196 <212> DNA <213> Homo sapien <400> 151 agegeggeag gteatattga acattecaga tacctateat tactegatge tgttgataac agcaagatgg ctttgaactc agggtcacca ccagctattg gaccttacta tgaaaaccat ggataccaac cggaaaaccc ctatcccgca cagcccactg tggtccccac tgtctacgag 180 gtgcatccgg ctcagt 196 <210> 152 <211> 132 <212> DNA <213> Homo sapien <400> 152 acagcacttt cacatgtaag aagggagaaa ttcctaaatg taggagaaag ataacagaac 60 cttccccttt tcatctagtg gtggaaacct gatgctttat gttgacagga atagaaccag 120 gagggagttt gt <210> 153 <211> 285 <212> DNA <213> Homo sapien <220> <221> misc\_feature <222> (1)...(285) <223> n = A,T,C or G<400> 153 acaanaccca nganaggcca ctggccgtgg tgtcatggcc tccaaacatg aaagtgtcag

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cttctgctct tatgtcctca tctgacaact ctttaccatt tttatcctcg ctcagcagga
                                                                        120
 gcacatcaat aaagtccaaa gtcttggact tggccttggc ttggaggaag tcatcaacac
                                                                        180
 cctggctagt gagggtgcgg cgccgctcct ggatgacggc atctgtgaag tcgtgcacca
                                                                        240
 gtctgcaggc cctgtggaag cgccgtccac acggagtnag gaatt
                                                                        285
       <210> 154
       <211> 333
       <212> DNA
       <213> Homo sapien
      <400> 154
accacagtcc tgttgggcca gggcttcatg accctttctg tgaaaagcca tattatcacc
                                                                         60
accccaaatt tttccttaaa tatctttaac tgaaggggtc agcctcttga ctgcaaagac
                                                                        120
cctaagccgg ttacacagct aactcccact ggccctgatt tgtgaaattg ctgctgcctg
                                                                        180
attggcacag gagtcgaagg tgttcagctc ccctcctccg tggaacgaga ctctgatttg
                                                                        240
agtttcacaa attctcgggc cacctcgtca ttgctcctct gaaataaaat ccggagaatg
                                                                        300
gtcaggcctg tctcatccat atggatcttc cgg
                                                                        333
      <210> 155
      <211> 308
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(308)
      <223> n = A,T,C or G
      <400> 155
actggaaata ataaaaccca catcacagtg ttgtgtcaaa gatcatcagg gcatggatgg
                                                                        60
gaaagtgctt tgggaactgt aaagtgccta acacatgatc gatgattttt gttataatat
                                                                       120
ttgaatcacg gtgcatacaa acteteetge etgeteetee tgggeeecag ecceagecee
                                                                       180
atcacagete actgetetgt teatecagge ceageatgta gtggetgatt ettettgget
                                                                       240
gcttttagcc tccanaagtt tctctgaagc caaccaaacc tctangtgta aggcatgctg
                                                                       300
gccctggt
                                                                       308
      <210> 156
      <211> 295
      <212> DNA
      <213> Homo sapien
      <400> 156
accttgctcg gtgcttggaa catattagga actcaaaata tgagatgata acagtgccta
ttattgatta ctgagagaac tgttagacat ttagttgaag attttctaca caggaactga
                                                                       120
gaataggaga ttatgtttgg ccctcatatt ctctcctatc ctccttgcct cattctatgt
                                                                       180
ctaatatatt ctcaatcaaa taaggttagc ataatcagga aatcgaccaa ataccaatat
                                                                       240
aaaaccagat gtctatcctt aagattttca aatagaaaac aaattaacag actat
                                                                       295
      <210> 157
      <211> 126
      <212> DNA
      <213> Homo sapien
     <400> 157
acaagtttaa atagtgctgt cactgtgcat gtgctgaaat gtgaaatcca ccacatttct
                                                                        60
```

```
gaagagcaaa acaaattctg tcatgtaatc tctatcttgg gtcgtgggta tatctgtccc
cttagt
                                                                        126
      <210> 158
      <211> 442
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(442)
      <223> n = A,T,C or G
      <400> 158
acceactggt cttggaaaca cccatcctta atacgatgat ttttctgtcg tgtgaaaatg
                                                                         60
aanccagcag gctgccccta gtcagtcctt ccttccagag aaaaagagat ttgagaaagt
                                                                        120
gcctgggtaa ttcaccatta atttcctccc ccaaactctc tgagtcttcc cttaatattt
                                                                       180
ctggtggttc tgaccaaagc aggtcatggt ttgttgagca tttgggatcc cagtgaagta
                                                                       240
natgtttgta gccttgcata cttagccctt cccacgcaca aacggagtgg cagagtggtg
                                                                       300
ccaaccctgt tttcccagtc cacgtagaca gattcacagt gcggaattct ggaagctgga
                                                                       360
nacagacggg ctctttgcag agccgggact ctgagangga catgagggcc tctgcctctg
                                                                       420
tgttcattct ctgatgtcct gt
                                                                       442
      <210> 159
      <211> 498
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1) ... (498)
      <223> n = A,T,C or G
      <400> 159
acttccaggt aacgttgttg tttccgttga gcctgaactg atgggtgacg ttgtaggttc
                                                                        60
tccaacaaga actgaggttg cagagegggt agggaagagt gctgttccag ttgcacctgg
                                                                       120
gctgctgtgg actgttgttg attcctcact acggcccaag gttgtggaac tggcanaaag
                                                                       180 .
gtgtgttgtt gganttgage tegggegget gtggtaggtt gtgggetett caacagggge
                                                                       240
tgctgtggtg ccgggangtg aangtgttgt gtcacttgag cttggccagc tctggaaagt
                                                                       300
antanattct tcctgaaggc cagcgcttgt ggagctggca ngggtcantg ttgtgtgtaa
                                                                       360
cgaaccagtg ctgctgtggg tgggtgtana tcctccacaa agcctgaagt tatggtgtcn
                                                                       420
tcaggtaana atgtggtttc agtgtccctg ggcngctgtg gaaggttgta nattgtcacc
                                                                       480
aagggaataa gctgtggt
                                                                       498
      <210> 160
      <211> 380
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(380)
      <223> n = A,T,C or G
      <400> 160
```

```
acctgcatcc agcttccctg ccaaactcac aaggagacat caacctctag acagggaaac
                                                                          .60
 agetteagga taetteeagg agacagagee accageagea aaacaaatat teecatgeet
                                                                         120
 ggagcatggc atagaggaag ctganaaatg tggggtctga ggaagccatt tgagtctggc
                                                                         180
 cactagacat ctcatcagcc acttgtgtga agagatgccc catgacccca gatgcctctc
                                                                         240 -
 ccaccettae etecatetea cacacttgag etttecaete tgtataatte taacateetg
                                                                         300
 gagaaaaatg gcagtttgac cgaacctgtt cacaacggta gaggctgatt tctaacgaaa
                                                                         360
 cttgtagaat gaagcctgga
                                                                         380
       <210> 161
       <211> 114
       <212> DNA
       <213> Homo sapien
       <400> 161
 actecacate ecetetgage aggeggttgt egtteaaggt gtatttggee ttgeetgtea
                                                                          60
 cactgtccac tggcccctta tccacttggt gcttaatccc tcgaaagagc atgt
                                                                         114
       <210> 162
       <211> 177
       <212> DNA
       <213> Homo sapien
       <400> 162
actttctgaa tcgaatcaaa tgatacttag tgtagtttta atatcctcat atatatcaaa
                                                                         60
gttttactac tctgataatt ttgtaaacca ggtaaccaga acatccagtc atacagcttt
                                                                         120
tggtgatata taacttggca ataacccagt ctggtgatac ataaaactac tcactgt
      <210> 163
      <211> 137
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1) ... (137)
      <223> n = A,T,C or G
      <400> 163
catttataca gacaggegtg aagacattca egacaaaaac gegaaattet ateeegtgac
                                                                         60
canagaaggc agctacggct actcctacat cctggcgtgg gtggccttcg cctgcacctt
                                                                        120
catcagcggc atgatgt
                                                                        137
      <210> 164
      <211> 469
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc feature
      <222> (1)...(469)
      \langle 223 \rangle n = A,T,C or G
      <400> 164
cttatcacaa tgaatgttct cctgggcagc gttgtgatct ttgccacctt cgtgacttta
tgcaatgcat catgctattt catacctaat gagggagttc caggagattc aaccaggaaa
```

```
tgcatggatc tcaaaggaaa caaacaccca ataaactcgg agtggcagac tgacaactgt
                                                                         180
 gagacatgca cttgctacga aacagaaatt tcatgttgca cccttgtttc tacacctgtg
                                                                         240
 ggttatgaca aagacaactg ccaaagaatc ttcaagaagg aggactgcaa gtatatcgtg
                                                                         300
 gtggagaaga aggacccaaa aaagacctgt tctgtcagtg aatggataat ctaatgtgct
                                                                         36.0
 tctagtaggc acagggctcc caggccaggc ctcattctcc tctggcctct aatagtcaat
                                                                         420
 gattgtgtag ccatgcctat cagtaaaaag atntttgagc aaacacttt
                                                                         469
       <210> 165
       <211> 195
       <212> DNA
       <213> Homo sapien
       <220>
       <221> misc_feature
       <222> (1) ... (195)
       <223> n = A,T,C or G
       <400> 165
acagtitttt atanatatcg acattgccgg cacttgtgtt cagtitcata aagctggtgg
atccgctgtc atccactatt ccttggctag agtaaaaatt attcttatag cccatgtccc
                                                                        120
tgcaggccgc ccgcccgtag ttctcgttcc agtcgtcttg gcacacaggg tgccaggact
                                                                        180
tcctctgaga tgagt
                                                                        195
      <210> 166
      <211> 383
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1) ... (383)
      <223> n = A,T,C or G
      <400> 166
acatettagt agtgtggcae atcaggggge cateagggte acagteacte atageetege
                                                                       60
cgaggtcgga gtccacacca ccggtgtagg tgtgctcaat cttgggcttg gcgccacct
                                                                        120
ttggagaagg gatatgctgc acacacatgt ccacaaagcc tgtgaactcg ccaaagaatt
                                                                        180
tttgcagacc agcctgagca aggggcggat gttcagcttc agctcctcct tcgtcaggtg
                                                                        240
gatgccaacc tegtetangg teegtgggaa getggtgtee aenteaceta caacetggge
                                                                        300
gangatetta taaagagget eenagataaa etecaegaaa ettetetggg agetgetagt
                                                                        360
nggggccttt ttggtgaact ttc
                                                                        383
      <210> 167 ·
      <211> 247
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(247)
      \langle 223 \rangle n = A,T,C or G
      <400> 167
acagagccag accttggcca taaatgaanc agagattaag actaaacccc aagtcganat
                                                                        60
tggagcagaa actggagcaa gaagtgggcc tggggctgaa gtagagacca aggccactgc
                                                                       120
```

```
tatanccata cacagagcca actctcaggc caaggcnatg gttggggcag anccagagac
                                                                          180
 tcaatctgan tccaaagtgg tggctggaac actggtcatg acanaggcag tgactctgac
                                                                          240
 tgangtc
                                                                          247
       <210> 168
       <211> 273
       <212> DNA
       <213> Homo sapien
       <220>
       <221> misc feature
       <222> (1)...(273)
       <223> n = A,T,C or G
       <400> 168
acttctaagt tttctagaag tggaaggatt gtantcatcc tgaaaatggg tttacttcaa
                                                                          60
 aatccctcan ccttgttctt cacnactgtc tatactgana gtgtcatgtt tccacaaagg
                                                                          120
gctgacacct gagcctgnat tttcactcat ccctgagaag ccctttccag tagggtgggc
                                                                         180
aattcccaac ttccttgcca caagcttccc aggctttctc ccctggaaaa ctccagcttg
                                                                         240
 agtcccagat acactcatgg gctgccctgg gca
                                                                         273
       <210> 169
      <211> 431
       <212> DNA
       <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1) ... (431)
      \langle 223 \rangle n = A,T,C or G
      <400> 169
acageettgg ettecceaaa etecacagte teagtgeaga aagateatet tecageagte
                                                                          60
agctcagacc agggtcaaag gatgtgacat caacagtttc tggtttcaga acaggttcta
                                                                         120
ctactgtcaa atgacccccc atacttcctc aaaggctgtg gtaagttttg cacaggtgag
                                                                         180
ggcagcagaa agggggtant tactgatgga caccatcttc tctgtatact ccacactgac
                                                                         240
cttgccatgg gcaaaggccc ctaccacaaa aacaatagga tcactgctgg gcaccagctc
                                                                         300
acgcacatca ctgacaaccg ggatggaaaa agaantgcca actttcatac atccaactgg
                                                                         360
aaagtgatct gatactggat tottaattac ottcaaaagc ttotgggggc catcagctgc
                                                                         420
tcgaacactg a
                                                                         431
      <210> 170
      <211> 266
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(266)
      \langle 223 \rangle n = A,T,C or G
      <400> 170
acctgtgggc tgggctgtta tgcctgtgcc ggctgctgaa agggagttca gaggtggagc
                                                                         60
tcaaggaget etgeaggeat tttgecaane etetecanag canagggage aacetacaet
                                                                        120
ccccgctaga aagacaccag attggagtcc tgggaggggg agttggggtg ggcatttgat
                                                                        180
```

```
gtatacttgt cacctgaatg aangagccag agaggaanga gacgaanatg anattggcct
tcaaagctag gggtctggca ggtgga
                                                                      266
      <210> 171
      <211> 1248
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc feature
      <222> (1)...(1248)
      \langle 223 \rangle n = A,T,C or G
      <400> 171
ggcagccaaa tcataaacgg cgaggactgc agcccgcact cgcagccctg gcaggcggca
                                                                       60
ctggtcatgg aaaacgaatt gttctgctcg ggcgtcctgg tgcatccgca gtgggtgctg
                                                                      120
tragccgcac actgtttcca gaagtgagtg cagageteet acaccategg getgggeetg
                                                                      180
cacagtettg aggeegacea agageeaggg ageeagatgg tggaggeeag ceteteegta
                                                                      240
cggcacccag agtacaacag accettgete getaacgace teatgeteat caagttggae
                                                                      300
gaatccgtgt ccgagtctga caccatccgg agcatcagca ttgcttcgca gtgccctacc
                                                                      360
gcggggaact cttgcctcgt ttctggctgg ggtctgctgg cgaacggcag aatgcctacc
                                                                      420 .
gtgctgcagt gcgtgaacgt gtcggtggtg tctgaggagg tctgcagtaa gctctatgac
                                                                      480
cegetgtace acceeageat gttetgegee ggeggaggge aagaceagaa ggacteetge
                                                                      540
aacggtgact ctggggggcc cetgatetgc aacgggtact tgcagggcct tgtqtctttc
                                                                      600
ggaaaagccc cgtgtggcca agttggcgtg ccaggtgtct acaccaacct ctgcaaattc
                                                                      660
actgagtgga tagagaaaac cgtccaggcc agttaactct ggggactggg aacccatgaa
                                                                      720
attgaccccc aaatacatcc tgcggaagga attcaggaat atctgttccc agcccctcct
                                                                      780
ccctcaggcc caggagtcca ggcccccagc ccctccccc tcaaaccaag ggtacagatc
                                                                      840
cccagcccct cctccctcag acccaggagt ccagaccccc cagcccctcc tccctcagac
                                                                      900
ccaggagtcc ageccetect cceteagace caggagteca gacceccag cccetectec
                                                                      960
ctcagaccca ggggtccagg cccccaaccc ctcctcctc agactcagag gtccaagccc
                                                                     1020.
ccaaccente attecceaga eccagaggte caggteccag eccetentee etcagaceca
geggtecaat gecaectaga etntecetgt acacagtgee ecettgtgge aegttgaece
                                                                     1140
aaccttacca gttggttttt catttttngt ccctttcccc tagatccaga aataaagttt
                                                                     1200
1248
      <210> 172
      <211> 159
      <212> PRT
      <213> Homo sapien
      <220>
      <221> VARIANT
      <222> (1)...(159)
      <223> Xaa = Any Amino Acid
      <400> 172
Met Val Glu Ala Ser Leu Ser Val Arg His Pro Glu Tyr Asn Arg Pro
                                   10
Leu Leu Ala Asn Asp Leu Met Leu Ile Lys Leu Asp Glu Ser Val Ser
                               25
Glu Ser Asp Thr Ile Arg Ser Ile Ser Ile Ala Ser Gln Cys Pro Thr
                           40
Ala Gly Asn Ser Cys Leu Val Ser Gly Trp Gly Leu Leu Ala Asn Gly
    50
                        55
```

```
Arg Met Pro Thr Val Leu Gln Cys Val Asn Val Ser Val Val Ser Glu
                    70
                                        75
Glu Val Cys Ser Lys Leu Tyr Asp Pro Leu Tyr His Pro Ser Met Phe
Cys Ala Gly Gly Gln Kaa Gln Kaa Asp Ser Cys Asn Gly Asp Ser
            100
                                105
                                                    110
Gly Gly Pro Leu Ile Cys Asn Gly Tyr Leu Gln Gly Leu Val Ser Phe
                            120
Gly Lys Ala Pro Cys Gly Gln Val Gly Val Pro Gly Val Tyr Thr Asn
                        135
                                            140
Leu Cys Lys Phe Thr Glu Trp Ile Glu Lys Thr Val Gln Ala Ser
                    150
                                        155
```

<210> 173

<211> 1265

<212> DNA

<213> Homo sapien

<220>

<221> misc\_feature

<222> (1)...(1265)

 $\langle 223 \rangle$  n = A,T,C or G

#### <400> 173

ggcagcccgc actegcagcc etggcaggcg gcactggtca tggaaaacga attgttctgc tegggegtee tggtgcatee geagtgggtg etgteageeg cacactgttt ecagaactee tacaccatcg ggctgggcct gcacagtctt gaggccgacc aagagccagg gagccagatg 180 gtggaggcca gcctctccgt acggcaccca gagtacaaca gacccttgct cgctaacgac 240 ctcatgctca tcaagttgga cgaatccgtg tccgagtctg acaccatccg gagcatcagc 300 attgcttcgc agtgccctac cgcggggaac tcttgcctcg tttctggctg gggtctgctg 360. gcgaacggtg agetcacggg tgtgtgtetg ceetetteaa ggaggteete tgcccagteg 420 cgggggctga cccagagctc tgcgtcccag gcagaatgcc taccgtgctg cagtgcgtga 480 acgtgtcggt ggtgtctgag gaggtctgca gtaagctcta tgacccgctg taccacccca 540 gcatgttctg cgccggcgga gggcaagacc agaaggactc ctgcaacggt gactctgggg 600 ggcccctgat ctgcaacggg tacttgcagg gccttgtgtc tttcggaaaa gccccgtgtg 660 gccaagttgg cgtgccaggt gtctacacca acctctgcaa attcactgag tggatagaga 720 aaaccgtcca ggccagttaa ctctggggac tgggaaccca tgaaattgac ccccaaatac 780 atcctgcgga aggaattcag gaatatctgt tcccagcccc tcctcctca ggcccaggag 840 tocaggecce cagecectee teecteaaac caagggtaca gatececage cetteetee 900 teagacecag gagtecagae eccecagece etectecete agacecagga gtecageoce 960 tecteentea gacceaggag tecagaceee ceageceete eteceteaga eccaggggtt 1020 gaggececca accectecte etteagagte agaggtecaa gececeaace ectegttece 1080 cagacccaga ggtnnaggtc ccagcccctc ttccntcaga cccagnggtc caatgccacc 1140 tagattttcc ctgnacacag tgcccccttg tggnangttg acceaacctt accagttggt 1200 ttttcatttt tngtcccttt cccctagatc cagaaataaa gtttaagaga ngngcaaaaa 1260 aaaaa 1265

<210> 174

<211> 1459

<212>. DNA

<213> Homo sapien

<220>

<221> misc\_feature

<222> (1)...(1459)

### $\langle 223 \rangle$ n = A,T,C or G

#### <400> 174

ggtcagccgc acactgtttc cagaagtgag tgcagagctc ctacaccatc gggctgggcc 60 tgcacagtct tgaggccgac caagagccag ggagccagat ggtggaggcc agcctctccg 120 tacggcaccc agagtacaac agaccettge tegetaacga ceteatgete atcaagttgg 180 acgaatccgt gtccgagtct gacaccatcc ggagcatcag cattgcttcg cagtgcccta -240 ccgcggggaa ctcttgcctc gtttctggct ggggtctgct ggcgaacggt gagctcacgg 300 gtgtgtgtct gccctcttca aggaggtcct ctgcccagtc gcgggggctg acccagagct 360 ctgcgtccca ggcagaatgc ctaccgtgct gcagtgcgtg aacgtgtcgg tggtgtctga 420 ngaggtetge antaagetet atgacceget gtaccacece ancatgttet gegeeggegg 480 agggcaagac cagaaggact cctgcaacgt gagagaggg aaaggggagg gcaggcgact 540 cagggaaggg tggagaaggg ggagacagag acacacaggg ccgcatggcg agatgcagag 600 atggagagac acacagggag acagtgacaa ctagagagag aaactgagag aaacagagaa 660 ataaacacag gaataaagag aagcaaagga agagagaaac agaaacagac atggggaggc 720 agaaacacac acacatagaa atgcagttga cettecaaca gcatggggcc tgagggcggt 780 gacctccacc caatagaaaa tcctcttata acttttgact ccccaaaaac ctgactagaa 840 atagcctact gttgacgggg agccttacca ataacataaa tagtcgattt atgcatacgt 900 tttatgcatt catgatatac ctttgttgga attttttgat atttctaagc tacacagttc 960 gtctgtgaat ttttttaaat tgttgcaact ctcctaaaat ttttctgatg tgtttattga 1020 aaaaatccaa gtataagtgg acttgtgcat tcaaaccagg gttgttcaag ggtcaactgt 1080 gtacccagag ggaaacagtg acacagattc atagaggtga aacacgaaga gaaacaggaa 1140 aaatcaagac tctacaaaga ggctgggcag ggtggctcat gcctgtaatc ccagcacttt 1200 gggaggcgag gcaggcagat cacttgaggt aaggagttca agaccagcct ggccaaaatg 1260 gtgaaatcct gtctgtacta aaaatacaaa agttagctgg atatggtggc aggcgcctgt 1320 aatcccagct acttgggagg ctgaggcagg agaattgctt gaatatggga ggcagaggtt 1380 gaagtgagtt gagatcacac cactatactc cagctggggc aacagagtaa gactctgtct 1440 Caaaaaaaa aaaaaaaaa 1459

<210> 175

<211> 1167

<212> DNA

<213> Homo sapien

<220>

<221> misc\_feature

<222> (1) ... (1167)

 $\langle 223 \rangle$  n = A,T,C or G

#### <400> 175

gcgcagccct ggcaggcggc actggtcatg gaaaacgaat tgttctgctc gggcgtcctg 60 gtgcatccgc agtgggtgct gtcagccgca cactgtttcc agaactccta caccatcggg 120 ctgggcctgc acagtcttga ggccgaccaa gagccaggga gccagatggt ggaggccagc 180 ctctccgtac ggcacccaga gtacaacaga ctcttgctcg ctaacgacct catgctcatc 240 aagttggacg aatccgtgtc cgagtctgac accatccgga gcatcagcat tgcttcgcag 300 tgccctaccg cggggaactc ttgcctcgtn tctggctggg gtctgctggc gaacggcaga 360 atgcctaccg tgctgcactg cgtgaacgtg tcggtggtgt ctgaggangt ctgcagtaag 420 ctctatgacc cgctgtacca ccccagcatg ttctgcgccg gcggagggca agaccagaag 480 gactcctgca acggtgactc tggggggccc ctgatctgca acgggtactt gcagggcctt 540 gtgtctttcg gaaaagcccc gtgtggccaa cttggcgtgc caggtgtcta caccaacctc 600 tgcaaattca ctgagtggat agagaaaacc gtccagncca gttaactctg gggactggga 660 acccatgaaa ttgaccccca aatacatcct gcggaangaa ttcaggaata tctgttccca 720 gcccctcctc cctcaggccc aggagtccag gcccccagcc cctcctccct caaaccaagg 780 gtacagatee ecageceete eteceteaga eccaggagte cagaeceece ageceetent 840 centeagace caggagteca geceetecte enteagacge aggagtecag acceecage 900

```
cententeeg teagaceeag gggtgeagge ecceaacee tenteentea gagteagagg
                                                                        960
 tccaagcccc caacccctcg ttccccagac ccagaggtnc aggtcccagc ccctcctccc
                                                                       1020
 tcagacccag cggtccaatg ccacctagan tntccctgta cacagtgccc ccttgtggca
                                                                       1080
 ngttgaccca accttaccag ttggtttttc atttttgtc cctttcccct agatccagaa
                                                                       1140
 ataaagtnta agagaagcgc aaaaaaa
                                                                       1167
       <210> 176
       <211> 205
       <212> PRT
       <213> Homo sapien
       <220>
       <221> VARIANT
       <222> (1)...(205)
       <223> Xaa = Any Amino Acid
       <400> 176
Met Glu Asn Glu Leu Phe Cys Ser Gly Val Leu Val His Pro Gln Trp
                                     10
Val Leu Ser Ala Ala His Cys Phe Gln Asn Ser Tyr Thr Ile Gly Leu
                                25
Gly Leu His Ser Leu Glu Ala Asp Gln Glu Pro Gly Ser Gln Met Val
                            40
Glu Ala Ser Leu Ser Val Arg His Pro Glu Tyr Asn Arg Leu Leu
                        55
Ala Asn Asp Leu Met Leu Ile Lys Leu Asp Glu Ser Val Ser Glu Ser
                    70
Asp Thr Ile Arg Ser Ile Ser Ile Ala Ser Gln Cys Pro Thr Ala Gly
                                    90
Asn Ser Cys Leu Val Ser Gly Trp Gly Leu Leu Ala Asn Gly Arg Met
            100
                                105
                                                    110
Pro Thr Val Leu His Cys Val Asn Val Ser Val Val Ser Glu Xaa Val
                            120
Cys Ser Lys Leu Tyr Asp Pro Leu Tyr His Pro Ser Met Phe Cys Ala
Gly Gly Gln Asp Gln Lys Asp Ser Cys Asn Gly Asp Ser Gly Gly
                    150
                                        155
Pro Leu Ile Cys Asn Gly Tyr Leu Gln Gly Leu Val Ser Phe Gly Lys
                                    170
Ala Pro Cys Gly Gln Leu Gly Val Pro Gly Val Tyr Thr Asn Leu Cys
                                185
Lys Phe Thr Glu Trp Ile Glu Lys Thr Val Gln Xaa Ser
        195
                            200
      <210> 177
      <211> 1119
      <212> DNA
      <213> Homo sapien
      <400> 177
gcgcactcgc agccctggca ggcggcactg gtcatggaaa acgaattgtt ctgctcgggc
                                                                       60
gtcctggtgc atccgcagtg ggtgctgtca gccgcacact gtttccagaa ctcctacacc
                                                                      120
ategggetgg geetgeacag tettgaggee gaccaagage cagggageea gatggtggag
                                                                      180
gccagcctct ccgtacggca cccagagtac aacagaccct tgctcgctaa cgacctcatg
                                                                      240
ctcatcaagt tggacgaatc cgtgtccgag tctgacacca tccggagcat cagcattgct
                                                                      300
```

```
tegeagtgee ctacegeggg gaactettge etegtttetg getggggtet getggegaac
                                                                       360
gatgctgtga ttgccatcca gtcccagact gtgggaggct gggagtgtga gaagctttcc
                                                                       420
caaccetgge agggttgtac cattteggea actteeagtg caaggacgte etgetgeate
                                                                       480
ctcactgggt gctcactact gctcactgca tcacccggaa cactgtgatc aactagccag
                                                                       540
caccatagtt ctccgaagtc agactatcat gattactgtg ttgactgtgc tgtctattgt
                                                                       600
actaaccatg ccgatgttta ggtgaaatta gcgtcacttg gcctcaacca tcttggtatc
                                                                       660
cagttatect caetgaattg agattteetg etteagtgte agecatteee acataattte
                                                                      -720
tgacctacag aggtgaggga tcatatagct cttcaaggat gctggtactc ccctcacaaa
                                                                      78.0
ttcatttctc ctgttgtagt gaaaggtgcg ccctctggag cctcccaggg tgggtgtgca
                                                                      840
ggtcacaatg atgaatgtat gatcgtgttc ccattaccca aagcctttaa atccctcatg
                                                                      900
ctcagtacac cagggcaggt ctagcatttc ttcatttagt gtatgctgtc cattcatgca
                                                                      960
accaccicag gacteetgga tictetgeet agitgagete eigeatgeig ecteetiggg
                                                                      1020
gaggtgaggg agagggccca tggttcaatg ggatctgtgc agttgtaaca cattaggtgc
                                                                     1080
ttaataaaca gaagctgtga tgttaaaaaa aaaaaaaaa
                                                                      1119
```

<210> 178

<211> 164

<212> PRT

<213> Homo sapien

<220>

<221> VARIANT

<222> (1) ... (164)

<223> Xaa = Any Amino Acid

#### <400> 178

Met Glu Asn Glu Leu Phe Cys Ser Gly Val Leu Val His Pro Gln Trp 10 Val Leu Ser Ala Ala His Cys Phe Gln Asn Ser Tyr Thr Ile Gly Leu 25 Gly Leu His Ser Leu Glu Ala Asp Gln Glu Pro Gly Ser Gln Met Val 40 Glu Ala Ser Leu Ser Val Arg His Pro Glu Tyr Asn Arg Pro Leu Leu 60 Ala Asn Asp Leu Met Leu Ile Lys Leu Asp Glu Ser Val Ser Glu Ser 75 Asp Thr Ile Arg Ser Ile Ser Ile Ala Ser Gln Cys Pro Thr Ala Gly 90 Asn Ser Cys Leu Val Ser Gly Trp Gly Leu Leu Ala Asn Asp Ala Val 105 Ile Ala Ile Gln Ser Xaa Thr Val Gly Gly Trp Glu Cys Glu Lys Leu 120 Ser Gln Pro Trp Gln Gly Cys Thr Ile Ser Ala Thr Ser Ser Ala Arg 135 140 Thr Ser Cys Cys Ile Leu Thr Gly Cys Ser Leu Leu Leu Thr Ala Ser 150 155 160 Pro Gly Thr Leu

<210> 179

<211> 250

<212> DNA

<213> Homo sapien

<400> 179

```
ctggagtgcc ttggtgtttc aagcccctgc aggaagcaga atgcaccttc tgaggcacct
                                                                            60
   ccagctgccc ccggccgggg gatgcgaggc tcggagcacc cttgcccggc tgtgattgct
                                                                           120
   gccaggcact gttcatctca gcttttctgt ccctttgctc ccggcaagcg cttctgctga
                                                                           180
   aagttcatat ctggagcctg atgtcttaac gaataaaggt cccatgctcc acccgaaaaa
                                                                           240
   aaaaaaaaa
                                                                           250
         <210> 180
         <211> 202
         <212> DNA
         <213> Homo sapien
         <400> 180
  actagtccag tgtggtggaa ttccattgtg ttgggcccaa cacaatggct acctttaaca
                                                                           60
tcacccagac cccgcccctg cccgtgcccc acgctgctgc taacgacagt atgatgctta
                                                                          120
  ctctgctact cggaaactat ttttatgtaa ttaatgtatg ctttcttgtt tataaatgcc
                                                                          180
  tgatttaaaa aaaaaaaaa aa
                                                                          202
         <210> 181
         <211> 558
         <212> DNA
         <213> Homo sapien
         <220>
        <221> misc_feature
        <222> (1)...(558)
        <223> n = A,T,C or G
        <400> 181
  tecyttigkt naggittikkg agacameeck agacetwaan eigigieaca gaetteyngg
                                                                           60
  aatgtttagg cagtgctagt aatttcytcg taatgattct gttattactt tcctnattct
                                                                          120
  ttattcctct ttcttctgaa gattaatgaa gttgaaaatt gaggtggata aatacaaaaa
                                                                          180
  ggtagtgtga tagtataagt atctaagtgc agatgaaagt gtgttatata tatccattca
                                                                          240
  aaattatgca agttagtaat tactcagggt taactaaatt actttaatat gctgttgaac
                                                                         300
  ctactctgtt ccttggctag aaaaaattat aaacaggact ttgttagttt gggaagccaa
                                                                          360
  attgataata ttctatgttc taaaagttgg gctatacata aattattaag aaatatggaw
                                                                          420
  ttttattccc aggaatatgg kgttcatttt atgaatatta cscrggatag awgtwtgagt
                                                                         480
  aaaaycagtt ttggtwaata ygtwaatatg tcmtaaataa acaakgcttt gacttatttc
                                                                         540
  caaaaaaaa aaaaaaaa
                                                                         558
        <210> 182
        <211> 479
        <212> DNA
        <213> Homo sapien
        <220>
        <221> misc_feature
        <222> (1) ... (479)
        \langle 223 \rangle n = A,T,C or G
        <400> 182
  acagggwttk grggatgcta agsccccrga rwtygtttga tccaaccctg gcttwttttc
  agaggggaaa atggggccta gaagttacag mscatytagy tggtgcgmtg gcacccctgg
                                                                         120
  esteacacag asteecgagt agetgggact acaggeacae agteactgaa geaggeectg
                                                                         180
  ttwgcaattc acgttgccac ctccaactta aacattcttc atatgtgatg tccttagtca
                                                                         240
  ctaaggttaa actttcccac ccagaaaagg caacttagat aaaatcttag agtactttca
                                                                         300
```

tactmttcta agtcctcttc cagcctcact kkgagtcctm cytgggggtt ga ntctcttggc tttctcaata aartctctat ycatctcatg tttaatttgg ta awtgstgara aaattaaaat gttctggtty mactttaaaa araaaaaaaa aa	cqcatara 420
<210> 183 <211> 384 <212> DNA <213> Homo sapien	
<400> 183	• •
aggcgggagc agaagctaaa gccaaagccc aagaagagtg gcagtgccag cad	tggtgcc 60
agtaccagta ccaataacag tgccagtgcc agtgccagca ccagtggtgg ctt	Cagtgct 120
ggtgccagcc tgaccgccac tctcacattt gggctcttcg ctggccttgg tgc	agetogt 180
gccagcacca gtggcagctc tggtgcctgt ggtttctcct acaagtgaga ttt	tagatat 240
tgttaatcct gccagtcttt ctcttcaagc cagggtgcat cctcagaaac cta	ictcaaca 300
cagcactcta ggcagccact atcaatcaat tgaagttgac actctgcatt ara	
3 ununununun unun	384
<210> 184	•
<211> 496	
<212> DNA	
<213> Homo sapien	
<220>	·
<221> misc_feature	•
<222> (1)(496)	: .
<223> n = A,T,C or G	
<400> 184	
accgaattgg gaccgctggc ttataagcga tcatgtyynt ccrgtatkac ctc	aacgagc 60
agggagatcg agtctatacg ctgaagaaat ttgacccgat gggacaacag acccccatcctgc tcggttctcc ccagatgaca aatactctsg acaccgaatc acc	tgctcag 120
aacgetteaa ggtgeteatg acceageac egegeeetgt cetetgaggg tee	atcaaga 180 cttaaac 240
tgatgtcttt tctgccacct gttacccctc ggagactccg taaccaaact ctt	cggactg 300
tgagccctga tgcctttttg ccagccatac tctttggcat ccagtctctc qtq	gcgattg 360
attatgettg tgtgaggeaa teatggtgge ateacceata aagggaacae att	100
	tgacttt 420
tttttctcat attttaaatt actacmagaw tattwmagaw waaatgawtt gaa	aaactst 480
tttttctcat attttaaatt actacmagaw tattwmagaw waaatgawtt gaa taaaaaaaaaaaaaaa '	aaactst 480 496
tttttctcat attttaaatt actacmagaw tattwmagaw waaatgawtt gaa taaaaaaaaaaaaaaa '	aaactst 480
tttttctcat attttaaatt actacmagaw tattwmagaw waaatgawtt gaa taaaaaaaaaaaaaa <210> 185	aaactst 480
tttttctcat attttaaatt actacmagaw tattwmagaw waaatgawtt gaa taaaaaaaaaaaaaaa '	aaactst 480
tttttctcat attttaaatt actacmagaw tattwmagaw waaatgawtt gaa taaaaaaaaa aaaaaa <210> 185	aaactst 480
tttttctcat attttaaatt actacmagaw tattwmagaw waaatgawtt gaa taaaaaaaaaaaaaaaaaaa	aaactst 480
tttttctcat attttaaatt actacmagaw tattwmagaw waaatgawtt gaa taaaaaaaaaaaaaaaaaaaaaaaaaaaaaaaa	480 496
tttttctcat attttaaatt actacmagaw tattwmagaw waaatgawtt gaa taaaaaaaaa aaaaaa  <210> 185 <211> 384 <212> DNA <213> Homo sapien  <400> 185 gctggtagcc tatggcgkgg cccacggagg ggctcctgag gccacggrac agte	aaactst 480 496
tttttctcat attttaaatt actacmagaw tattwmagaw waaatgawtt gaa taaaaaaaaa aaaaaa  <210> 185	gacttcc 60
tttttctcat attttaaatt actacmagaw tattwmagaw waaatgawtt gaa taaaaaaaaa aaaaaa  <210> 185 <211> 384 <212> DNA <213> Homo sapien  <400> 185 gctggtagcc tatggcgkgg cccacggagg ggctcctgag gccacggrac agtgcaagtatcyt gcgcsgcgtc ttctaccgtc cctacctgca gatcttcggg cagaaggaggacat ggacgtggcc ctcatggagc acagcaactg ytcgtcggag ccca	gacttcc 60 attcccc 120 agcttct 180
tttttctcat attttaaatt actacmagaw tattwmagaw waaatgawtt gaa taaaaaaaaaaaaaaaaaaaaaaaaaaaaaaaa	gacttcc 60 attcccc 120 agcttct 180 agcttcc 240
tttttctcat attttaaatt actacmagaw tattwmagaw waaatgawtt gaa taaaaaaaaaaaaaaaaaaaaaaaaaaaaaaaa	gacttcc 60 attcccc 120 ggcttct 180 eggctgg 240 attcctca 300
tttttctcat attttaaatt actacmagaw tattwmagaw waaatgawtt gaa taaaaaaaaaaaaaaaaaaaaaaaaaaaaaaaa	gacttcc 60 attcccc 120 ggcttct 180 eggctgg 240 attcctca 300
tttttctcat attttaaatt actacmagaw tattwmagaw waaatgawtt gaa taaaaaaaaa aaaaaa  <210> 185 <211> 384 <212> DNA <213> Homo sapien  <400> 185 gctggtagcc tatggcgkgg cccacggagg ggctcctgag gccacggrac agtcaagtatcyt gcgcsgcgtc ttctaccgtc cctacctgca gatcttcggg cagaggaggacat ggacgtggcc ctcatggagc acagcaactg ytcgtcggag cccgggagaggacaccc tcctggggcc caggcggca cctgcgtctc ccagtatgcc aact tggtgctgct cctcgtcatc ttcctgctcg tggccaacat cctgctggtc aact ttgccatgtt cagttacaca ttcggcaaag tacagggcaa cagcgatctc tact gcgcagcgtt accgcctcat ccgg	gacttcc 60 attcccc 120 agcttct 180 agcttct 300 atgggaag 360
tttttctcat attttaaatt actacmagaw tattwmagaw waaatgawtt gaa taaaaaaaaaaaaaaaaaaaaaaaaaaaaaaaa	gacttcc 60 attcccc 120 agcttct 180 agcttct 300 atgggaag 360

```
<212> DNA
       <213> Homo sapien
       <220>
       <221> misc_feature
       <222> (1) ... (577)
       <223> n = A,T,C or G
       <400> 186
 gagttagete etecacaace ttgatgaggt egtetgeagt ggeetetege tteatacege
                                                                          60
 tnccatcgtc atactgtagg tttgccacca cytcctggca tcttggggcg gcntaatatt
                                                                         120
 ccaggaaact ctcaatcaag tcaccgtcga tgaaacctgt gggctggttc tgtcttccgc
                                                                         180
 teggtgtgaa aggatetece agaaggagtg etegatette eccaeaettt tgatgaettt
                                                                         240
 attgagtcga ttctgcatgt ccagcaggag gttgtaccag ctctctgaca gtgaggtcac
                                                                         300
cagccctatc atgccgttga mcgtgccgaa garcaccgag ccttgtgtgg gggkkgaagt
                                                                         360
ctcacccaga ttctgcatta ccagagagec gtggcaaaag acattgacaa actcgcccag
                                                                         420
gtggaaaaag amcamctcct ggargtgctn gccgctcctc gtcmgttggt ggcagcgctw
                                                                         480
tccttttgac acacaaacaa gttaaaggca ttttcagccc ccagaaantt gtcatcatcc
                                                                         540.
aagatntcgc acagcactna tccagttggg attaaat
                                                                         577
       <210> 187
       <211> 534
       <212> DNA
       <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1) ... (534)
      \langle 223 \rangle n = A,T,C or G
      <400> 187
aacatcttcc tgtataatgc tgtgtaatat cgatccgatn ttgtctgstg agaatycatw
                                                                         60
actkggaaaa gmaacattaa agcctggaca ctggtattaa aattcacaat atgcaacact
                                                                        120
ttaaacagtg tgtcaatctg ctcccyynac tttgtcatca ccagtctggg aakaagggta
                                                                        180
tgccctattc acacctgtta aaagggcgct aagcattttt gattcaacat ctttttttt
                                                                        240
gacacaagtc cgaaaaaagc aaaagtaaac agttatyaat ttgttagcca attcactttc
                                                                        300
ttcatgggac agagccatyt gatttaaaaa gcaaattgca taatattgag cttygggagc
                                                                        360
tgatatttga geggaagagt ageettteta etteaecaga cacaacteee ttteatattg
                                                                        420
ggatgttnac naaagtwatg tctctwacag atgggatgct tttgtggcaa ttctgttctg
                                                                        480
aggatetece agtttattta ceaettgeae aagaaggegt tttetteete agge
                                                                        534
      <210> 188
      <211> 761
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(761)
      \langle 223 \rangle n = A,T,C or G
      <400> 188
agaaaccagt atctctnaaa acaacctctc ataccttgtg gacctaattt tgtgtgcgtg
                                                                         60
tgtgtgtgcg cgcatattat atagacaggc acatcttttt tacttttgta aaagcttatg
                                                                        120
cctctttggt atctatatct gtgaaagttt taatgatctg ccataatgtc ttggggacct
                                                                        180
```

<212> DNA

```
ttgtcttctg tgtaaatggt actagagaaa acacctatnt tatgagtcaa tctagttngt
                                                                       240
tttattcgac atgaaggaaa tttccagatn acaacactna caaactctcc ctkqackarq
                                                                       300
ggggacaaag aaaagcaaaa ctgamcataa raaacaatwa cctggtgaga arttgcataa
                                                                       360
acagaaatwr ggtagtatat tgaarnacag catcattaaa rmgttwtktt wttctccctt
                                                                       420
gcaaaaaaca tgtacngact tcccgttgag taatgccaag ttgtttttt tatnataaaa
                                                                       480
cttgcccttc attacatgtt tnaaagtggt gtggtgggcc aaaatattga aatgatggaa
                                                                       540
ctgactgata aagctgtaca aataagcagt gtgcctaaca agcaacacag taatqttgac
                                                                       600
atgcttaatt cacaaatgct aatttcatta taaatgtttg ctaaaataca ctttgaacta
                                                                       660
tttttctgtn ttcccagagc tgagatntta gattttatgt agtatnaagt gaaaaantac
                                                                       720
gaaaataata acattgaaga aaaananaaa aaanaaaaaa a
      <210> 189
      <211> 482
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(482)
      \langle 223 \rangle n = A,T,C or G
      <400> 189
ttttttttt tttgccgatn ctactatttt attgcaggan gtgggggtgt atgcaccgca
caccggggct atnagaagca agaaggaagg agggagggca cagcccttg ctgagcaaca
aagccgcctg ctgccttctc tgtctgtctc ctggtgcagg cacatgggga gaccttcccc
                                                                       180
aaggcagggg ccaccagtcc aggggtggga atacaggggg tgggangtgt gcataagaag
                                                                       240
tgataggcac aggccacccg gtacagaccc ctcggctcct gacaggtnga tttcgaccag
                                                                       300
gtcattgtgc cctgcccagg cacagcgtan atctggaaaa gacagaatgc tttccttttc
                                                                       360
aaatttggct ngtcatngaa ngggcanttt tccaanttng gctnggtctt ggtacncttg
                                                                       420
gttcggccca gctccncgtc caaaaantat tcacccnnct ccnaattgct tgcnggnccc
                                                                      480
      <210> 190
      <211> 471
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(471)
      <223> n = A,T,C or G
      <400> 190
tttttttttt ttttaaaaca gtttttcaca acaaaattta ttagaagaat agtggttttg
aaaactctcg catccagtga gaactaccat acaccacatt acagctngga atgtnctcca
                                                                      120
aatgtctggt caaatgatac aatggaacca ttcaatctta cacatgcacg aaagaacaag
                                                                      180
cgcttttgac atacaatgca caaaaaaaaa agggggggg gaccacatgg attaaaattt
                                                                      240
taagtactca tcacatacat taagacacag ttctagtcca gtcnaaaatc agaactgcnt
                                                                      300
tgaaaaattt catgtatgca atccaaccaa agaacttnat tggtgatcat gantnotcta
                                                                      360
ctacatcnac cttgatcatt gccaggaacn aaaagttnaa ancacncngt acaaaaanaa
                                                                      420
tctgtaattn anttcaacct ccgtacngaa aaatnttnnt tatacactcc c
                                                                      471
      <210> 191
      <211> 402
```

```
<213> Homo sapien
       <220>
       <221> misc_feature
       <222> (1) ... (402)
       \langle 223 \rangle n = A,T,C or G
       <400> 191
 gagggattga aggtctgttc tastgtcggm ctgttcagcc accaactcta acaagttgct
                                                                          60
 gtcttccact cactgtctgt aagcttttta acccagacwg tatcttcata aatagaacaa
                                                                         120
 attetteace agteacatet tetaggacet tittggatte agttagtata agetetteca
                                                                         180
 cttcctttgt taagacttca tctggtaaag tcttaagttt tgtagaaagg aattyaattg
                                                                         240
 ctcgttctct aacaatgtcc tctccttgaa gtatttggct gaacaaccca cctaaagtcc
                                                                         300
 ctttgtgcat ccattttaaa tatacttaat agggcattgk tncactaggt taaattctgc
                                                                         360
 aagagtcatc tgtctgcaaa agttgcgtta gtatatctgc ca
                                                                         402
       <210> 192
       <211> 601
       <212> DNA
       <213> Homo sapien
       <220>
       <221> misc_feature
       <222> (1) ... (601)
       \langle 223 \rangle n = A,T,C or G
       <400> 192
gageteggat ecaataatet ttgtetgagg geageacaea tatneagtge catggnaact
                                                                          60
ggtctacccc acatgggagc agcatgccgt agntatataa ggtcattccc tgagtcagac
                                                                         120
atgcytyttt gaytaccgtg tgccaagtgc tggtgattct yaacacacyt ccatcccgyt
                                                                         180
cttttgtgga aaaactggca cttktctgga actagcarga catcacttac aaattcaccc
                                                                         240
acgagacact tgaaaggtgt aacaaagcga ytcttgcatt gctttttgtc cctccggcac
                                                                         300
cagttgtcaa tactaacccg ctggtttgcc tccatcacat ttgtgatctg tagctctgga
                                                                         360
tacatctcct gacagtactg aagaacttct tettttgttt caaaagcare tettggtgee
                                                                         420
tgttggatca ggttcccatt tcccagtcyg aatgttcaca tggcatattt wacttcccac
                                                                         480
aaaacattgc gatttgaggc tcagcaacag caaatcctgt tccggcattg gctgcaagag
                                                                         540
cctcgatgta gccggccagc gccaaggcag gcgccgtgag ccccaccagc agcagaagca
                                                                         600
                                                                         601
      <210> 193
      <211> 608
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1) ... (608)
      <223> n = A,T,C or G
      <400> 193
atacagecca nateceacca egaagatgeg ettgttgaet gagaacetga tgeggteact
                                                                         60
ggtcccgctg tagccccagc gactctccac ctgctggaag cggttgatgc tgcactcytt
                                                                        120
cccaacgcag gcagmagcgg gsccggtcaa tgaactccay tcgtggcttg gggtkgacgg
                                                                        180
tkaagtgcag gaagaggctg accacctcgc ggtccaccag gatgcccgac tgtgcgggac
                                                                        240
ctgcagcgaa actectcgat ggtcatgagc gggaagcgaa tgaggcccag ggccttgccc
                                                                        300
```

```
agaaccttcc gcctgttctc tggcgtcacc tgcagctgct gccgctgaca ctcggcctcg
gaccagegga caaacggcrt tgaacagecg caceteaegg atgeecagtg tgtegegete
                                                                        420
caggammgsc accagcgtgt ccaggtcaat gtcggtgaag ccctccgcgg gtratggcgt
                                                                        480
ctgcagtgtt tttgtcgatg ttctccaggc acaggctggc cagctgcggt tcatcgaaga
                                                                        540
gtcgcgcctg cgtgagcagc atgaaggcgt tgtcggctcg cagttcttct tcaggaactc
                                                                        600
cacgcaat
                                                                        608
      <210> 194
      <211> 392
      <212> DNA
       <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(392)
      <223> n = A,T,C or G
      <400> 194
gaacggctgg accttgcctc gcattgtgct tgctggcagg gaataccttg gcaagcagyt
                                                                        60
ccagtccgag cagccccaga ccgctgccgc ccgaagctaa gcctgcctct ggccttcccc
                                                                       120
tccgcctcaa tgcagaacca gtagtgggag cactgtgttt agagttaaga gtgaacactg
                                                                       180
tttgatttta cttgggaatt tcctctgtta tatagctttt cccaatgcta atttccaaac
                                                                       240
aacaacaaca aaataacatg tttgcctgtt aagttgtata aaagtaggtg attctgtatt
                                                                       300
taaagaaaat attactgtta catatactgc ttgcaatttc tgtatttatt gktnctstgg
                                                                       360
aaataaatat agttattaaa ggttgtcant cc
                                                                       392
      <210> 195
      <211> 502
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1) ... (502)
      <223> n = A,T,C or G
      <400> 195
ccsttkgagg ggtkaggkyc cagttyccga gtggaagaaa caggccagga gaagtgcgtg
                                                                        60
ccgagctgag gcagatgttc ccacagtgac ccccagagcc stgggstata gtytctgacc
                                                                       120
cctcncaagg aaagaccacs ttctggggac atgggctgga gggcaggacc tagaggcacc
                                                                       180
aagggaagge cccattccgg ggstgttccc cgaggaggaa gggaaggggc tctgtgtgcc
                                                                       240
ccccasgagg aagaggccct gagtcctggg atcagacacc ccttcacgtg tatccccaca
                                                                       300
caaatgcaag ctcaccaagg tcccctctca gtccccttcc stacaccctg amcggccact
                                                                       360
gscscacacc cacccagage acgccacccg ccatggggar tgtgctcaag gartcgcngg
                                                                       420
gcarcgtgga catcingtcc cagaaggggg cagaatctcc aatagangga cigarcmstt
                                                                       480
gctnanaaaa aaaaanaaaa aa
                                                                       502
      <210> 196
      <211> 665
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1) ... (665)
```

# <223> n = A,T,C or G

<400> 196	
ggttacttgg tttcattgcc accacttagt ggatgtc	att tagaaccatt ttgtctgctc 6
cctctggaag ccttgcgcag agcggacttt gtaattg	ttg gagaataact getgaatttt 120
wagctgtttk gagttgatts gcaccactgc acccaca	act tcaatatgaa aacyawttga 180
actwatttat tatcttgtga aaagtataac aatgaaa	att ttgttcatac tgtattkatc 240
aagtatgatg aaaagcaawa gatatatatt cttttat	tat gttaaattat gattgccatt 300
attaatcggc aaaatgtgga gtgtatgttc ttttcac	agt astatators tittetaset
tcacttggtt attttattgt aaatgartta caaaatt	agt aatatatgcc ttttgtaact 360
watattatt tcattaattt ctttcctkgt ttacgtw	Ctt aatttaagar aatggtatgt 420
tcttgacaga aatcgatctt gatgctgtgg aagtagt	aat tiigaaaaga wigcaigait 48( tig acccacaicc claigagitt 54(
ttcttagaat gtataaaggt tgtagcccat cnaactt	Cas acceptant carragets 540
tttgcaatca ggctgaaatg tggcatgctn ttctaat	caa agaaaaaaat gaccacatac
aagtg	665
	. 663
<210> 197	·
<211> 492	
<212> DNA	
<213> Homo sapien	
<220>	
<221> misc_feature	
<222> (1) (492)	• •
$\langle 223 \rangle$ n = A,T,C or G	•
<400> 197	
ttttnttttt tttttttgc aggaaggatt ccattta	tg tggatgcatt ttcacaatat 60
atgtttattg gagcgatcca ttatcagtga aaagtatc	caa gtgtttataa natttttagg 120
aaggcagatt cacagaacat gctngtcngc ttgcagtt	tt acctcgtana gatnacagag 180
aattatagtc naaccagtaa acnaggaatt tactttt	caa aagattaaat ccaaactgaa 240
caaaattcta ccctgaaact tactccatcc aaatattc	ga ataanagtca gcagtgatac 300
attetettet gaactttaga ttttetagaa aaatatgt	aa tagtgatcag gaagagctct 360
tgttcaaaag tacaacnaag caatgttccc ttaccata	agg ccttaattca aactttgatc 420
catttcactc ccatcacggg agtcaatgct acctggga	ica cttgtatttt gttcatnctg 480
ancntggctt aa	492
<210> 198	*
<211> 478	-
<212> DNA	
<213> Homo sapien	•
	•
<220>	
<221> misc_feature	
<222> (1)(478)	
<223> n = A,T,C or G	·
<400> 198	
tttnttttgn atttcantct gtannaanta ttttcatt	at gtttattana aaaatatnaa 60
tgtntccacn acaaatcatn ttacntnagt aagaggcc	an ctacattota caacatacac 120
tgagtatatt ttgaaaagga caagtttaaa gtanacno	at attgccganc atancacatt 180
tatacatggc ttgattgata tttagcacag canaaact	ga gtgagttacc agaaanaaat 240
natatatgtc aatcngattt aagatacaaa acagatcc	ta tggtacatan catchtgtag 300
gagttgtggc tttatgttta ctgaaagtca atgcagtt	CC tgtacaaaga gatggccqta 360
agcattctag tacctctact ccatggttaa gaatcgta	ca cttatgttta catatgtnca 420

```
gggtaagaat tgtgttaagt naanttatgg agaggtccan gagaaaaatt tgatncaa
                                                                         478
       <210> 199
       <211> 482
       <212> DNA
       <213> Homo sapien
       <220>
       <221> misc feature
       <222> (1) ... (482)
       \langle 223 \rangle n = A,T,C or G
       <400> 199
agtgacttgt cctccaacaa aaccccttga tcaagtttgt ggcactgaca atcagaccta
                                                                         60
tgctagttcc tgtcatctat tcgctactaa atgcagactg gaggggacca aaaaggggca
tcaactccag ctggattatt ttggagcctg caaatctatt cctacttgta cggactttga
                                                                        180
agtgattcag tttcctctac ggatgagaga ctggctcaag aatatcctca tgcagcttta
                                                                        240
tgaagccnac tctgaacacg ctggttatct nagatgagaa ncagagaaat aaagtcnaga
                                                                        300
aaatttacct ggangaaaag aggetttngg etggggacca teccattgaa eettetetta
                                                                        360
anggacttta agaanaaact accacatgtn tgtngtatcc tggtgccngg ccgtttantg
                                                                        420
aachtngach neaccettht ggaatanant ettgachgen teetgaactt geteetetge
                                                                        480
       <210> 200
       <211> 270
       <212> DNA
       <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1) ... (270)
      <223> n = A,T,C or G
      <400> 200
cggccgcaag tgcaactcca gctggggccg tgcggacgaa gattctgcca gcagttggtc
                                                                        60
cgactgcgac gacggcggcg gcgacagtcg caggtgcagc gcgggcgcct ggggtcttgc
                                                                        120
aaggetgage tgaegeegea gaggtegtgt caegteecae gaeettgaeg eegtegggga
                                                                        180
cageeggaac agageeeggt gaangeggga ggeetegggg ageeeetegg gaagggegge
                                                                        240
ccgagagata cgcaggtgca ggtggccgcc
                                                                        270
      <210> 201
      <211> 419
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1) ... (419)
      <223> n = A,T,C or G
      <400> 201
ttttttttt ttttggaate tactgegage acageaggte ageaacaagt ttattttgca
                                                                        60
gctagcaagg taacagggta gggcatggtt acatgttcag gtcaacttcc tttgtcgtgg
                                                                       120
ttgattggtt tgtctttatg ggggcggggt ggggtagggg aaancgaagc anaantaaca
                                                                        180
tggagtgggt gcaccctccc tgtagaacct ggttacnaaa gcttggggca gttcacctgg
                                                                        240
```

```
tctgtgaccg tcattttctt gacatcaatg ttattagaag tcaggatatc ttttagagag
                                                                      300
 tccactgtnt ctggagggag attagggttt cttgccaana tccaancaaa atccacntga
                                                                      360
 aaaagttgga tgatncangt acngaatacc ganggcatan ttctcatant cggtggcca
                                                                      419
       <210> 202
       <211> 509
       <212> DNA
       <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(509)
      <223> n = A,T,C or G
      <400> 202
60
tggcacttaa tccattttta tttcaaaatg tctacaaant ttnaatncnc cattatacng
                                                                     120
gtnattttnc aaaatctaaa nnttattcaa atntnageca aanteettae neaaatnnaa
                                                                     180
tacneneaaa aateaaaaat ataentntet tteageaaae ttngttacat aaattaaaaa
                                                                     240
aatatatacg gctggtgttt tcaaagtaca attatcttaa cactgcaaac atntttnnaa
                                                                     300
ggaactaaaa taaaaaaaaa cactnccgca aaggttaaag ggaacaacaa attcntttta
                                                                     360
caacancnnc nattataaaa atcatatete aaatettagg ggaatatata etteacaeng
                                                                     420
ggatcttaac ttttactnca ctttgtttat ttttttanaa ccattgtntt gggcccaaca
                                                                     480
caatggnaat necneenene tggactagt
                                                                     509
      <210> 203
      <211> 583
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature -
      <222> (1) . . . (583)
      <223> n = A,T,C or G
      <400> 203
ttttttttt tttttttga cccccctctt ataaaaaaca agttaccatt ttattttact
                                                                     60 .
tacacatatt tattttataa ttggtattag atattcaaaa ggcagctttt aaaatcaaac
                                                                    120
taaatggaaa ctgccttaga tacataattc ttaggaatta gcttaaaatc tgcctaaagt
                                                                    180
gaaaatcttc tctagctctt ttgactgtaa atttttgact cttgtaaaac atccaaattc
                                                                    240
atttttcttg tctttaaaat tatctaatct ttccattttt tccctattcc aagtcaattt
                                                                    300
gcttctctag cctcatttcc tagctcttat ctactattag taagtggctt ttttcctaaa
                                                                    360
agggaaaaca ggaagagana atggcacaca aaacaaacat tttatattca tatttctacc
                                                                    420
tacgttaata aaatagcatt ttgtgaagcc agctcaaaag aaggcttaga tccttttatg
                                                                    480
tccattttag tcactaaacg atatcnaaag tgccagaatg caaaaggttt gtgaacattt
                                                                    540
attcaaaagc taatataaga tatttcacat actcatcttt ctg
                                                                    583
     <210> 204
     <211> 589
     <212> DNA
     <213> Homo sapien
     <220>
     <221> misc_feature
     <222> (1)...(589)
```

480

#### <223> n = A,T,C or G

```
<400> 204
ttttttttt tttttttt ttttttctc ttctttttt ttganaatga ggatcgagtt
                                                                         60
tttcactctc tagatagggc atgaagaaaa ctcatctttc cagctttaaa ataacaatca
                                                                        120
aatotottat gotatatoat attttaagtt aaactaatga gtoactggot tatototoo
                                                                        180
tgaaggaaat ctgttcattc ttctcattca tatagttata tcaagtacta ccttgcatat
                                                                      -240
tgagaggttt ttcttctcta tttacacata tatttccatg tgaatttgta tcaaaccttt
                                                                       300
attttcatgc aaactagaaa ataatgtntt cttttgcata agagaagaga acaatatnag
                                                                       360
cattacaaaa ctgctcaaat tgtttgttaa gnttatccat tataattagt tnggcaggag
                                                                       420
ctaatacaaa tcacatttac ngacnagcaa taataaaact gaagtaccag ttaaatatcc
                                                                       480
aaaataatta aaggaacatt tttagcctgg gtataattag ctaattcact ttacaagcat
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     <210> 205
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      <212> DNA
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      <220>
      <221> misc_feature
      <222> (1) ... (545)
      <223> n = A,T,C or G
      <400> 205
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                                                                        60
agaaaagtgc cttacattta ataaaagttt gtttctcaaa gtgatcagag gaattagata
                                                                       120
tngtcttgaa caccaatatt aatttgagga aaatacacca aaatacatta agtaaattat
                                                                       180
ttaagatcat agagcttyta agtgaaaaga taaaatttya cctcagaaac tctgagcatt
aaaaatccac tattagcaaa taaattacta tggacttett getttaattt tgtgatgaat
                                                                       300
atggggtgtc actggtaaac caacacattc tgaaggatac attacttagt gatagattct
                                                                       360
tatgtacttt gctanatnac gtggatatga gttgacaagt ttctctttct tcaatctttt
                                                                       420
aaggggcnga ngaaatgagg aagaaaagaa aaggattacg catactgttc tttctatngg
                                                                       480
aaggattaga tatgtttcct ttgccaatat taaaaaaaata ataatgttta ctactagtga
                                                                       540
aaccc
      <210> 206
      <211> 487
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1) ... (487)
      \langle 223 \rangle n = A,T,C or G
      <400> 206
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                                                                        60
catttattag ctctgcaact tacatattta aattaaagaa acgttnttag acaactgtna
                                                                       120
caatttataa atgtaaggtg ccattattga gtanatatat tcctccaaga gtggatgtgt
                                                                       180
cccttctccc accaactaat gaancagcaa cattagttta attttattag tagatnatac
                                                                       240
actgctgcaa acgctaattc tcttctccat ccccatgtng atattgtgta tatgtgtgag
                                                                       300
ttggtnagaa tgcatcanca atctnacaat caacagcaag atgaagctag gcntgggctt
                                                                       360
tcggtgaaaa tagactgtgt ctgtctgaat caaatgatct gacctatcct cggtggcaag
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```

aactettega acegetteet caaaggenge tgecacattt gtggentetn ttgcacttgt

```
ttcaaaa
                                                                          487
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       <211> 332
       <212> DNA
       <213> Homo sapien
       <220>
       <221> misc_feature
       <222> (1) ... (332)
       \langle 223 \rangle n = A,T,C or G
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tacatagcat taaatcccaa atcctattta aagacctgac agcttgagaa ggtcactact
                                                                         120
gcatttatag gaccttctgg tggttctgct gttacntttg aantctgaca atccttgana
                                                                         180
atctttgcat gcagaggagg taaaaggtat tggattttca cagaggaana acacagggca
                                                                         240
gaaatgaagg ggccaggctt actgagcttg tccactggag ggctcatggg tgggacatgg
                                                                         300
aaaagaaggc agcctaggcc ctggggagcc ca
                                                                         332
      <210> 208
      <211> 524
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc feature
      <222> (1) . . . (524)
      \langle 223 \rangle n = A,T,C or G
      <400> 208
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gttgtgttcc ggccccatcc aaccacgaag ttgatttctc ttgtgtgcag agtgactgat
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tttaaaggac atggagcttg tcacaatgtc acaatgtcac agtgtgaagg gcacactcac
                                                                         180
tcccgcgtga ttcacattta gcaaccaaca atagctcatg agtccatact tgtaaatact
                                                                         240
tttggcagaa tacttnttga aacttgcaga tgataactaa gatccaagat atttcccaaa
                                                                         300
gtaaatagaa gtgggtcata atattaatta cctgttcaca tcagcttcca tttacaagtc
                                                                         360
atgageceag acaetgaeat caaactaage ceaettagae teetcaecae cagtetgtee
                                                                         420
tgtcatcaga caggaggctg tcaccttgac caaattctca ccagtcaatc atctatccaa
                                                                         480
aaaccattac ctgatccact tccggtaatg caccaccttg gtga
                                                                         524
      <210> 209
      <211> 159
      <212> DNA
      <213> Homo sapien
      <400> 209
gggtgaggaa atccagagtt gccatggaga aaattccagt gtcagcattc ttgctccttg
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tggccctctc ctacactctg gccagagata ccacagtcaa acctggagcc aaaaaggaca
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caaaggactc tcgacccaaa ctgccccaga ccctctcca
                                                                        159
      <210> 210
      <211> 256
      <212> DNA
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<213> Homo sapien

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<220>
       <221> misc_feature
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       <223> n = A,T,C or G
       <400> 210
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tggggagatt ttanccaatt tangtntgta aatggggaga ctggggcagg cgggagagat
                                                                         180
ttgcagggtg naaatgggan ggctggtttg ttanatgaac agggacatag gaggtaggca
                                                                         240
ccaggatgct aaatca
                                                                         256
      <210> 211
      <211> 264
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc feature
      <222> (1) ... (264)
      \langle 223 \rangle n = A,T,C or G
      <400> 211
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actggaacac atacccacat ctttgttctg agggataatt ttctgataaa gtcttgctgt
                                                                        120
atattcaagc acatatgtta tatattattc agttccatgt ttatagccta gttaaggaga
                                                                        180
ggggagatac attcngaaag aggactgaaa gaaatactca agtnggaaaa cagaaaaaga
                                                                        240
aaaaaaggag caaatgagaa gcct
      <210> 212
      <211> 328
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1) ... (328)
      <223> n = A, T, C or G
     <400> 212
acccaaaaat ccaatgctga atatttggct tcattattcc canattcttt gattgtcaaa
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ggatttaatg ttgtctcagc ttgggcactt cagttaggac ctaaggatgc cagccggcag
                                                                        120
gtttatatat gcagcaacaa tattcaagcg cgacaacagg ttattgaact tgcccgccag
ttnaatttca ttcccattga cttgggatcc ttatcatcag ccagagagat tgaaaattta
                                                                        240
cccctacnac tetttactet etgganaggg ccagtggtgg tagetataag ettggccaca
                                                                       300
ttttttttc ctttattcct ttgtcaga
      <210> 213
      <211> 250
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc feature
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<222> (1)...(250)
         \langle 223 \rangle n = A,T,C or G
         <400> 213
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   taaagcattg ctcactgaag ggatagaagt gactgccagg agggaaagta agccaaggct
                                                                            120
   cattatgcca aagganatat acatttcaat tctccaaact tcttcctcat tccaagagtt
                                                                            180
   ttcaatattt gcatgaacct gctgataanc catgttaana aacaaatatc tctctnacct
                                                                            240
   tctcatcggt
                                                                            250
         <210> 214
         <211> 444
         <212> DNA
         <213> Homo sapien
         <220>
         <221> misc_feature
         <222> (1)...(444)
         \langle 223 \rangle n = A,T,C or G
         <400> 214
   acccagaatc caatgctgaa tatttggctt cattattccc agattctttg attgtcaaag
                                                                            60
   gatttaatgt tgtctcagct tgggcacttc agttaggacc taaggatgcc agccggcagg
                                                                           120
  tttatatatg cagcaacaat attcaagcgc gacaacaggt tattgaactt gcccgccagt
                                                                            180
   tgaatttcat toccattgac ttgggatcct tatcatcagc canagagatt gaaaatttac
                                                                            240
  ccctacgact ctttactctc tggagagggc cagtggtggt agctataagc ttggccacat
                                                                           300
  ttttttttcc tttattcctt tgtcagagat gcgattcatc catatgctan aaaccaacag
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  agtgactttt acaaaattcc tataganatt gtgaataaaa ccttacctat agttgccatt
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  actttgctct ccctaatata cctc
         <210> 215
         <211> 366
         <212> DNA
        <213> Homo sapien
        <220>
        <221> misc_feature
        <222> (1) ... (366)
        \langle 223 \rangle n = A,T,C or G
        <400> 215
  acttatgage agagegacat atccaagtgt anactgaata aaactgaatt ctctccagtt
                                                                            60
  taaagcattg ctcactgaag ggatagaagt gactgccagg agggaaagta agccaaggct
                                                                           120
cattatgcca aagganatat acatttcaat tctccaaact tcttcctcat tccaagagtt
                                                                           180
  ttcaatattt gcatgaacct gctgataagc catgttgaga aacaaatatc tctctgacet
                                                                           240
  tctcatcggt aagcagaggc tgtaggcaac atggaccata gcgaanaaaa aacttagtaa
                                                                           300
  tccaagctgt tttctacact gtaaccaggt ttccaaccaa ggtggaaatc tcctatactt
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  ggtgcc
                                                                           366
        <210> 216
        <211> 260
        <212> DNA
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<220>

<213> Homo sapien

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<221> misc_feature
       <222> (1)...(260)
       \langle 223 \rangle n = A,T,C or G
       <400> 216
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 caagacaggg gcctaaggag ggtctccaca ctgctnntaa gggctnttnc attttttat
                                                                         -120
 taataaaaag tnnaaaaggc ctcttctcaa cttttttccc ttnggctgga aaatttaaaa
                                                                         180
 atcaaaaatt teetnaagtt nteaagetat catatataet ntateetgaa aaageaacat
                                                                         240
 aattetteet teeeteett
                                                                         260
       <210> 217
       <211> 262
       <212> DNA
       <213> Homo sapien
       <220>
       <221> misc_feature
       <222> (1) ... (262)
       <223> n = A,T,C or G
      <400> 217
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tcttgcctat aattttctat tttaataagg aaatagcaaa ttggggtggg gggaatgtag
                                                                         120
ggcattctac agtttgagca aaatgcaatt aaatgtggaa ggacagcact gaaaaatttt
                                                                         180
atgaataatc tgtatgatta tatgtctcta gagtagattt ataattagcc acttacccta
                                                                         240
atateettea tgettgtaaa gt
                                                                        262
      <210> 218
      <211> 205
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1) ... (205)
      <223> n = A,T,C or G
      <400> 218.
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                                                                         60
cccctatcaa ctcccttttg tagtaaactt ggaaccttgg aaatgaccag gccaagactc
                                                                        120
aggecteece agttetactg acetttgtee ttangtntna ngtecagggt tgetaggaaa
                                                                        180
anaaatcagc agacacaggt gtaaa
                                                                        205
      <210> 219
      <211> 114
      <212> DNA
      <213> Homo sapien
      <400> 219
tactgttttg tctcagtaac aataaataca aaaagactgg ttgtgttccg gccccatcca
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accacgaagt tgatttctct tgtgtgcaga gtgactgatt ttaaaggaca tgga
                                                                        114
      <210> 220
      <211> 93
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<212> DNA
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 aaataagcat ttagtgctca gtccctactg agt
                                                                          93
      <210> 221
       <211> 167
       <212> DNA
       <213> Homo sapien
      <220>
      <221> misc_feature
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      \langle 223 \rangle n = A,T,C or G
      <400> 221
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tettttgece ageetgtgge tetactgtag taagtttetg etgatgagga geeagnatge
                                                                      120
ccccactac cttccctgac gctccccana aatcacccaa cctctgt
                                                                        .167
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      <211> 351
      <212> DNA
      <213> Homo sapien
      <400> 222
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gttcttcacc tgtcccccaa tccttaaaag gccatactgc ataaagtcaa caacagataa
                                                                        120
atgtttgctg aattaaagga tggatgaaaa aaattaataa tgaatttttg cataatccaa
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ttttctcttt tatatttcta gaagaagttt ctttgagcct attagatccc gggaatcttt
                                                                        240
taggtgagca tgattagaga gcttgtaggt tgcttttaca tatatctggc atatttgagt
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ctcgtatcaa aacaatagat tggtaaaggt ggtattattg tattgataag t
                                                                        351
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      <211> 383
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      <220>
      <221> misc_feature
      <222> (1)...(383)
      \langle 223 \rangle n = A,T,C or G
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                                                                        120
ttaaaatgtc tgtgccaaaa ttttgtattt tatttggaga cttcttatca aaagtaatgc
                                                                        180
tgccaaagga agtctaagga attagtagtg ttcccmtcac ttgtttggag tgtgctattc
                                                                       240
taaaagattt tgatttcctg gaatgacaat tatattttaa ctttggtggg ggaaanagtt
                                                                       300
ataggaccac agtetteact tetgatactt gtaaattaat ettttattge acttgttttg
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accattaagc tatatgttta aaa
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       <400> 224
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                                                                     120
 ggatacatgg ttaaaggata raagggcaat attttatcat atgttctaaa agagaaggaa
                                                                      180
 gagaaaatac tactttctcr aaatggaagc ccttaaaggt gctttgatac tgaaggacac
                                                                      240
 aaatgtggcc gtccatcctc ctttaragtt gcatgacttg gacacggtaa ctgttgcagt
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aactcctaca ccatcgggct gggcctgcac agtcttgagg ccgaccaaga gccagggagc
                                                                     180
cagatggtgg aggccagcct ctccgtacgg cacccagagt acaacagacc cttgctcgct
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                                                                    1020
gtcccagccc ctcctccctc agacccagcg gtccaatgcc acctagactc tccctgtaca
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1200
aaaaaaaaa aaaa
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agaacctggc ccagtcataa tcattcatcc tgacagtggc aataatcacg ataaccagt
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     <212> DNA
     <213> Homo sapien
     <400> 227
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Table Nome Bapt				: :	:
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caggaactee aagteeacat cettggeaac tggggaettg egeaggttag cettgaggat	120
ggcaacacgg gacttctcat caggaagtgg gatgtagatg agctgatcaa gacggccagg	180
tctgaggatg gcaggatcaa tgatgtcagg ccggttggta ccgccaatga tgaacacatt	240
tttttttgtg gacatgccat ccatttctgt caggatctgg ttgatgactc ggtcagcagc	300
C	301
0.0	•
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<400> 232	
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management and a second	120
agaagagtee atetgetgtg aaggagagae agagaaetet gggtteegte gteetgteea	180
cgtgctgtac caagtgctgg tgccagcctg ttacctgttc tcactgaaaa tctggctaat	240
gctcttgtgt atcacttctg attctgacaa tcaatcaatc aatggcctag agcactgact	300
	300 301
g	
g <210> 233	
g <210> 233 <211> 301	
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g <210> 233 <211> 301	
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<pre></pre>	
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<pre></pre>	60 120
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301
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        <211> 283
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        <213> Homo sapien
        <400> 235
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 aattccctca tcttttaggg aatcatttac caggtttgga gaggattcag acagctcagg
                                                                         120
 tgctttcact aatgtctctg aacttctgtc cctctttgtt catggatagt ccaataaata
                                                                         180
 atgttatctt tgaactgatg ctcataggag agaatataag aactctgagt gatatcaaca
                                                                         240
 ttagggattc aaagaaatat tagatttaag ctcacactgg tca
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       <210> 236
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       <212> DNA
       <213> Homo sapien
       <400> 236
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 aatactttta aatcgatcag atttccctaa cccacatgca atcttcttca ccagaagagg
                                                                        120
 teggageage ateattaata ceaageagaa tgegtaatag ataaatacaa tggtatatag
                                                                        180
 tgggtagacg gcttcatgag tacagtgtac tgtggtatcg taatctggac ttgggttgta
                                                                        240
 aagcatcgtg taccagtcag aaagcatcaa tactcgacat gaacgaatat aaagaacacc
                                                                        300
                                                                        301
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       <211> 301
       <212> DNA
       <213> Homo sapien
       <400> 237
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                                                                       120
ccttggctaa tgcctcatag taggagtcct cagaccagcc atggggatca aacatatcct
                                                                       180
ttgggtagtt ggtgccaagc tcgtcaatgg cacagaatgg atcagcttct cgtaaatcta
                                                                       240
gggttccgaa attetttett cetttggata atgtagttca tatccattce etectttate
                                                                       300
                                                                       301
      <210> 238
      <211> 301
      <212> DNA
      <213> Homo sapien
      <400> 238
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                                                                       120
cettgagaet teeggagteg aggeteteea gggtteecea geceateaat cattttetge
                                                                       180
accccctgcc tgggaagcag ctccctgggg ggtgggaatg ggtgactaga agggatttca
                                                                       240
gtgtgggacc cagggtctgt tcttcacagt aggaggtgga agggatgact aatttcttta
                                                                       300
                                                                       301
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BAICDOOID, MIC. COOK AND

<210> 239 <211> 239

<212> DNA <213> Homo sapien <400> 239 ataagcagct agggaattct ttatttagta atgtcctaac ataaaagttc acataactgc ttctgtcaaa ccatgatact gagctttgtg acaacccaga aataactaag agaaggcaaa cataatacct tagagatcaa gaaacattta cacagttcaa ctgtttaaaa atagctcaac 180 attcagccag tgagtagagt gtgaatgcca gcatacacag tatacaggtc cttcaggga <210> 240 <211> 300 <212> DNA <213> Homo sapien <400> 240 ggtcctaatg aagcagcagc ttccacattt taacgcaggt ttacggtgat actgtccttt gggatctgcc ctccagtgga accttttaag gaagaagtgg gcccaagcta agttccacat gctgggtgag ccagatgact tctgttccct ggtcactttc ttcaatgggg cgaatggggg ctgccaggtt tttaaaatca tgcttcatct tgaagcacac ggtcacttca ccctcctcac 240 gctgtgggtg tactttgatg aaaataccca ctttgttggc ctttctgaag ctataatgtc <210> 241 <211> 301 <212> DNA <213> Homo sapien <400> 241 gaggtctggt gctgaggtct ctgggctagg aagaggagtt ctgtggagct ggaagccaga 60 cetetttgga ggaaacteca geagetatgt tggtgtetet gagggaatge aacaaggetg 120 ctcctccatg tattggaaaa ctgcaaactg gactcaactg gaaggaagtg ctgctgccag tgtgaagaac cagcctgagg tgacagaaac ggaagcaaac aggaacagcc agtctttct tectectet gteataeggt eteteteaag cateetttgt tgteagggge etaaaaggga 300 301 <210> 242 <211> 301 <212> DNA <213> Homo sapien <400> 242 ccgaggtcct gggatgcaac caatcactct gtttcacgtg acttttatca ccatacaatt 60 tgtggcattt cctcattttc tacattgtag aatcaagagt gtaaataaat gtatatcgat 120 gtcttcaaga atatatcatt cctttttcac tagaacccat tcaaaatata agtcaagaat 180 cttaatatca acaaatatat caagcaaact ggaaggcaga ataactacca taatttagta 240 taagtaccca aagttttata aatcaaaagc cctaatgata accattttta gaattcaatc 300 <210> 243 <211> 301 <212>. DNA <213> Homo sapien <400> 243 aggtaagtcc cagtttgaag ctcaaaagat ctggtatgag cataggctca tcgacgacat 60 ggtggcccaa gctatgaaat cagagggagg cttcatctgg gcctgtaaaa actatgatgg 120

3	
tgacgtgcag tcggactctg tggcccaagg gtatggctct ctcggcatga tgaccagcgt	180
yctggtttgt ccagatggca agacagtaga agcagaggct gcccacggga ctgtaaccg	240
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t	301
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greatycaat eccattigea ggatetgtet gtgeacatge etetgtagag accaggates	. 120
ccayyyacci tygadacagi tgacacigia aqqiqciiqc tccccaagac acargornaa	180
aggreetiged diggreeded collections of the collection of the collec	240
actgtttgtc ttttgtgtat cttttttaaa ctgtaaagtt caattgtgaa aatgaatatc	300
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<211> 301	•• .
<212> DNA	÷
<213> Homo sapien	
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adgecagga gatatigica tiaatgiara citcaggaca ciagagiata geaggectar	180
gttttcaaag agcagagatg caattaaata ttgtttagca tcaaaaaggc cactcaatac	240
agctaataaa atgaaagacc taatttetaa agcaattett tataatttac aaagttttaa	300
g	301
<210> 246	•
<210> 246 <211> 301	
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<213> Homo sapien	•
(213) Nomo Sapten	
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acctgggctt attttaaaga actatttgta gctcagattg gttttcctat ggctaaaata	120
agtgettett gtgaaaatta aataaaacag ttaatteaaa geettgatat atgttaceac	180
taacaatcat actaaatata ttttgaagta caaagtttga catgctctaa agtgacaacc	240
caaatgtgtc ttacaaaaca cgttcctaac aaggtatgct ttacactacc aatgcagaaa	300
	301
<210> 247	
<211> 301	
<212> DNA	
<213> Homo.sapien	
nomo : sahren.	•
<400> 247	٠
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gcctaagagg gcgactggcg gcagcacaac caaggaaggc aaggttgttt cccccacgct	120
gtgtcctgtg ttcaggtgcg acacacaatc ctcatgggaa caggatcacc catgcgctgc	180
corrected caaggregg gorraagtgg attaagggag qcaagttotg ggrecorec	240
cttttcaaac catgaagtca ggctctgtat ccctcctttt cctaactgat attctaacta	300
a · · · · · · · · · · · · · · · · · · ·	301
	•

<210> 252 <211> 301

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<210> 248
       <211> 301
       <212> DNA
       <213> Homo sapien
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 attaggaaga ttcttagggg taatttttct gaggaaggag aactagccaa cttaagaatt
                                                                        120
acaggaagaa agtggtttgg aagacagcca aagaaataaa agcagattaa attgtatcag
                                                                        180
gtacattcca gcctgttggc aactccataa aaacatttca gattttaatc ccgaatttag
                                                                        240
ctaatgagac tggatttttg ttttttatgt tgtgtgtcgc agagctaaaa actcagttcc
                                                                        300
                                                                        301
      <210> 249
      <211> 301
       <212> DNA
       <213> Homo sapien
      <400> 249
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                                                                       60
ecctgacget getgttetee cegaaaaace egacegacet cegegatete egteeegee
                                                                       120
ccagggagac acagcagtga ctcagagctg gtcgcacact gtgcctccct cctcaccgcc
                                                                       180
catcgtaatg aattattttg aaaattaatt ccaccatcct ttcagattct ggatggaaag
                                                                       240
actgaatctt tgactcagaa ttgtttgctg aaaagaatga tgtgactttc ttagtcattt
                                                                       300
                                                                       301
      <210> 250
      <211> 301
      <212> DNA
      <213> Homo sapien
      <400> 250
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cttatettta tiggetigat aaacataati attietaaca etagettati teeagtigee
                                                                      - 120
cataagcaca tcagtacttt tctctggctg gaatagtaaa ctaaagtatg gtacatctac
                                                                       180
ctaaaagact actatgtgga ataatacata ctaatgaagt attacatgat ttaaagacta
                                                                       240
caataaaacc aaacatgctt ataacattaa gaaaaacaat aaagatacat gattgaaacc
                                                                       300.
                                                                       301
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     <211> 301
      <212> DNA
      <213> Homo sapien
      <400> 251
geogaggice tacattigge coagitteee cotgeatest etecagggee cotgeeteat
                                                                        60
agacaacete atagageata ggagaactgg ttgeeetggg ggeaggggga etgtetggat
                                                                       120
ggcaggggtc ctcaaaaatg ccactgtcac tgccaggaaa tgcttctgag cagtacacct
                                                                       180
cattgggatc aatgaaaagc ttcaagaaat cttcaggctc actctcttga aggcccggaa
                                                                       240
cctctggagg ggggcagtgg aatcccagct ccaggacgga tcctgtcgaa aagatatcct
                                                                       300
                                                                       301
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<212> DNA

60

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<213> Homo sapien
        <400> 252
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  ttttctacat tgtagaatca agagtgtaaa taaatgtata tcgatgtctt caagaatata
  tcattccttt ttcactagga acccattcaa aatataagtc aagaatctta atatcaacaa
                                                                         120
  atatatcaag caaactggaa ggcagaataa ctaccataat ttagtataag tacccaaagt
                                                                         180
  tttataaatc aaaagcccta atgataacca tttttagaat tcaatcatca ctgtagaatc
                                                                         240
                                                                         300
                                                                         301
        <210> 253
       <211> 301
       <212> DNA
       <213> Homo sapien
     ·· <400> 253
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 caactaaaaa aaaaaaataa agaaaaaatg tgctgcgttc tgaaaaataa ctccttagct
                                                                         60
 tggtctgatt gttttcagac cttaaaatat aaacttgttt cacaagettt aatecatgtg
                                                                        120
 gattttttt cttagagaac cacaaaacat aaaaggagca agtcggactg aatacctgtt
                                                                        180
 tecatagige ecacagggia tiecteacat titetecata ggaaaatget titteecaag
                                                                        300
                                                                        301
       <210> 254
       <211> 301
       <212> DNA
       <213> Homo sapien
      <400> 254
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aacttgacca attcccttga agcgggtggg ttaaaccctg taaatgggaa caaaatcccc
                                                                        60
ccaaatctct tcatcttacc ctggtggact cctgactgta gaattttttg gttgaaacaa
                                                                       120
gaaaaaaata aagetttgga ettttcaagg ttgettaaca ggtaetgaaa gaetggeete
                                                                       180
acttaaactg agccaggaaa agctgcagat ttattaatgg gtgtgttagt gtgcagtgcc
                                                                       240
                                                                       300
                                                                       301
      <210> 255
      <211> 302
      <212> DNA
      <213> Homo sapien
     <400> 255
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attactgaaa tgtttctttt ctgaatataa atataaatat gtgcaaagtt tgacttggat
                                                                       60
tgggattttg ttgagttctt caagcatctc ctaataccct caagggcctg agtaggggg
                                                                       120
aggaaaaagg actggaggtg gaatctttat aaaaaacaag agtgattgag gcagattgta
                                                                       180
aacattatta aaaaacaaga aacaaacaaa aaaatagaga aaaaaaccac cccaacacac
                                                                      240
                                                                      300
                                                                      302
      <210> 256
     <211> 301
     <212> DNA
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       <222> (1)...(301)
       <223> n = A,T,C or G
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                                                                        60
aggaccetee tecceacace teaatecace aaaccateca taatgeacee agataggeee
                                                                        120
acccccaaaa gcctggacac cttgagcaca cagttatgac caggacagac tcatctctat
                                                                        180
aggcaaatag ctgctggcaa actggcatta cctggtttgt ggggatgggg gggcaagtgt
                                                                        240..
gtggcctctc ggcctggtta gcaagaacat tcagggtagg cctaagttan tcgtgttagt
                                                                        300
                                                                        301
      <210> 257
      <211> 301
      <212> DNA
      <213> Homo sapien
      <400> 257
gttgtggagg aactetgget tgeteattaa gteetaetga tttteactat ceeetgaatt
                                                                         60
tececaetta tttttgtett teaetatege aggeettaga agaggtetae etgeeteeag
                                                                        120
tettacetag tecagtetae eccetggagt tagaatggee atcetgaagt gaaaagtaat
                                                                        180
gtcacattac tecetteagt gatttettgt agaagtgeea atecetgaat gecaceaaga
                                                                        240
tettaatett cacatettta atettatete tttgacteet etttacaceg gagaaggete
                                                                        300
                                                                        301
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      <211> 301
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(301)
      <223> n = A,T,C or G
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aggggcccag ccaccaggcg cagaagcaag ataaacagta ggctcaagac cagagccacc
                                                                       120
cccagggcaa caagaatcca ataccaggac tgggcaaaat cttcaaagat cttaacactg
                                                                       180
atgtctcggg cattgaggct gtcaataana cgctgatccc ctgctgtatg gtggtgtcat
                                                                       240
tggtgatccc tgggagcgcc ggtggagtaa cgttggtcca tggaaagcag cgcccacaac
                                                                       300
                                                                       301
     <210> 259
      <211> 301
      <212> DNA
      <213> Homo sapien
     <220>
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     <222> (1)...(301)
     <223> n = A,T,C or G
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<400> 259

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tcatatatgc aaacaaatgc agactangcc tcaggcagag actaaaggac atctcttggg
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                                                                         120
 gcaaagccat aaggaagccc aggattcctt gtgatcagga agtgggccag gaaggtctgt
                                                                         180
 tccagctcac atctcatctg catgcagcac ggaccggatg cgcccactgg gtcttggctt
                                                                         240
 ccctcccatc ttctcaagca gtgtccttgt tgagccattt gcatccttgg ctccaggtgg
                                                                         300
                                                                         301.
       <210> 260
       <211> 301
       <212> DNA
       <213> Homo sapien
       <400> 260
 ttttttttt ccctaaggaa aaagaaggaa caagtctcat aaaaccaaat aagcaatggt
                                                                         60
 aaggtgtctt aacttgaaaa agattaggag tcactggttt acaagttata attgaatgaa
                                                                        120
 agaactgtaa cagccacagt tggccatttc atgccaatgg cagcaaacaa caggattaac
                                                                        180
 tagggcaaaa taaataagtg tgtggaagcc ctgataagtg cttaataaac agactgattc
                                                                        240
 actgagacat cagtacetge eegggeggee getegageeg aattetgeag atatecatea
                                                                        300
                                                                        301
       <210> 261
       <211> 301
       <212> DNA
       <213> Homo sapien
      <400> 261
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                                                                         60
tetgetteca tecaegatte tageaatgae eteteggaea teaaagetee tettaaggtt
                                                                       120
agcaccaact attccataca attcatcagc aggaaataaa ggctcttcag aaggttcaat
                                                                       180
ggtgacatcc aatttcttct gataatttag attcctcaca accttcctag ttaagtgaag
                                                                       240
ggcatgatga tcatccaaag cccagtggtc acttactcca gactttctgc aatgaagatc
                                                                       300
                                                                       301
      <210> 262
      <211> 301
      <212> DNA
      <213> Homo sapien
      <400> 262
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                                                                        60
tgtgagette ttgeegeaag teteteagaa atttaaaaag atgeaaatee etgagteace
                                                                       120
cctagacttc ctaaaccaga tcctctgggg ctggaacctg gcactctgca tttgtaatga
                                                                       180
gggctttctg gtgcacacct aattttgtgc atctttgccc taaatcctgg attagtgcoc
                                                                       240
catcattace eccacattat aatgggatag atteagagea gatactetee ageaaagaat
                                                                       300
                                                                       301
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      <211> 301
      <212> DNA
     <213> Homo sapien
     <220>
     <221> misc_feature
     <222> (1)...(301)
     <223> n = A,T,C or G
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 aaaattacta cttaatccta attcacaata acaatggcat taaggtttga cttgagttgg
                                                                          60 -
 ttcttagtat tatttatggt aaataggctc ttaccacttg caaataactg gccacatcat
                                                                         120
                                                                         180
 taatgactga cttcccagta aggctctcta aggggtaagt angaggatcc acaggatttg
 agatgctaag gccccagaga tcgtttgatc caaccctctt attttcagag gggaaaatgg
                                                                         240
                                                                         300
                                                                         301
       <210> 264
       <211> 301
       <212> DNA
       <213> Homo sapien-
       <400> 264
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 aatgaatgac tctaaaaaca atatttacat ttaatggttt gtagacaata aaaaaacaag
                                                                         60
 gtggatagat ctagaattgt aacattttaa gaaaaccata scatttgaca gatgagaaag
                                                                        120
 ctcaattata gatgcaaagt tataactaaa ctactatagt agtaaagaaa tacatttcac
                                                                        180
 accetteata taaatteaet atettggett gaggeaetee ataaaatgta teaegtgeat
                                                                        240
                                                                        300
                                                                        301
       <210> 265
       <211> 301
       <212> DNA
       <213> Homo sapien
     <400> 265
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cttcttgtga cgcagtattt cttctctggg gagaagccgg gaagtcttct cctggctcta
                                                                         60
catattettg gaagteteta atcaactttt gttecatttg ttteatttet teaggaggga
                                                                       120
ttttcagttt gtcaacatgt tctctaacaa cacttgccca tttctgtaaa gaatccaaag
                                                                       180
cagtccaagg ctttgacatg tcaacaacca gcataactag agtatccttc agagatacgg
                                                                       240
                                                                       300
                                                                       301
      <210> 266
      <211> 301
      <212> DNA
      <213> Homo sapien
    <400> 266
taccgtctgc cettectece atccaggeca tetgegaate tacatgggte etectatteg
                                                                        60
acaccagate actettteet etacceacag gettgetatg ageaagagae acaaceteet
ctcttctgtg ttccagcttc ttttcctgtt cttcccaccc cttaagttct attcctgggg
                                                                       120
atagagacac caatacccat aacctctctc ctaagcctcc ttataaccca gggtgcacag
                                                                       180
                                                                       240
cacagactee tgacaactgg taaggeeaat gaactgggag etcacagetg getgtgeetg
                                                                       300
                                                                       301
      <210> 267
      <211> 301
      <212> DNA
     <213> Homo sapien
     <400> 267
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aaagagcaca ggccagctca gcctgccctg gccatctaga ctcagcctgg ctccatgggg

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gttctcagtg ctgagtccat ccaggaaaag ctcacctaga ccttctgagg ctgaatcttc
                                                                         120
 atcctcacag gcagcttctg agagcctgat attcctagcc ttgatggtct ggagtaaagc
                                                                         180
 ctcattctga ttcctctcct tcttttcttt caagttggct ttcctcacat ccctctgttc
                                                                         240
 aattogotto agottgtotg otttagooot catttocaga agottottot otttggcato
                                                                         300 -
                                                                         301
       <210> 268
       <211> 301
       <212> DNA
       <213> Homo sapien
       <400> 268
aatgtctcac tcaactactt cccagcctac cgtggcctaa ttctgggagt tttcttctta
                                                                         60
gatettggga gagetggtte ttetaaggag aaggaggaag gacagatgta aetttggate
                                                                        120
tcgaagagga agtctaatgg aagtaattag tcaacggtcc ttgtttagac tcttggaata
                                                                        180
tgctgggtgg ctcagtgagc ccttttggag aaagcaagta ttattcttaa ggagtaacca
                                                                        240
cttcccattg ttctactttc taccatcatc aattgtatat tatgtattct ttggagaact
                                                                        300
                                                                        301
      <210> 269
      <211> 301
      <212> DNA
      <213> Homo sapien
      <400> 269
taacaatata cactagetat etttttaact greeateatt ageaceaatg aagatreaat
                                                                         60
aaaattacct ttattcacac atctcaaaac aattctgcaa attcttagtg aagtttaact
                                                                        120
atagtcacag accttaaata ttcacattgt tttctatgtc tactgaaaat aagttcacta
                                                                        180
cttttctgga tattctttac aaaatcttat taaaattcct ggtattatca ccccaatta
                                                                        240
tacagtagca caaccacctt atgtagtttt tacatgatag ctctgtagaa gtttcacatc
                                                                        300
                                                                        301
      <210> 270
      <211> 301
      <212> DNA
      <213> Homo sapien
      <400> 270
cattgaagag cttttgcgaa acatcagaac acaagtgctt ataaaattaa ttaagcctta
                                                                        60
cacaagaata catatteett ttatttetaa ggagttaaac atagatgtag etgatgtgga
                                                                       120
gagettgetg gtgcagtgca tattggataa cactatteat ggccgaattg atcaagtcaa
                                                                       180
ccaactcctt gaactggatc atcagaagaa gggtggtgca cgatatactg cactagataa
                                                                       240
tggaccaacc aactaaattc tctcaccagg ctgtatcagt aaactggctt aacagaaaac
                                                                       300
                                                                       301
      <210> 271
      <211> 301
      <212> DNA
      <213> Homo sapien
      <220>
     <221> misc_feature
     <222> (1) ... (301)
     <223> n = A, T, C or G
```

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<400> 271
  aaaaggttct cataagatta acaatttaaa taaatatttg atagaacatt ctttctcatt
                                                                           60
  tttatagctc atctttaggg ttgatattca gttcatgctt cccttgctgt tcttgatcca
                                                                          120
  gaattgcaat cacttcatca gcctgtattc gctccaattc tctataaagt gggtccaagg
                                                                          180
  tgaaccacag agccacagca cacctettte cettggtgae tgcetteace ceatganggt
                                                                          240
  tetetectee agatganaac tgateatgeg cecacatttt gggttttata gaageagtea
                                                                          300
                                                                          301
        <210> 272
        <211> 301
        <212> DNA
        <213> Homo sapien
        <400> 272
  taaattgcta agccacagat aacaccaatc aaatggaaca aatcactgtc ttcaaatgtc
  ttatcagaaa accaaatgag cctggaatct tcataatacc taaacatgcc gtatttagga
                                                                          60
                                                                         120
  tccaataatt ccctcatgat gagcaagaaa aattctttgc gcacccctcc tgcatccaca
                                                                         180
  gcatcttctc caacaaatat aacettgagt ggcttcttgt aatctatgtt ctttgttttc
  ctaaggactt ccattgcatc tcctacaata ttttctctac gcaccactag aattaagcag
                                                                         240
                                                                         300
                                                                         301
        <210> 273
        <211> 301
       <212> DNA
        <213> Homo sapien
       <220>
       <221> misc_feature
       <222> (1)...(301)
       <223> n = A,T,C or G
       <400> 273
 acatgtgtgt atgtgtatct ttgggaaaan aanaagacat cttgtttayt attttttgg
                                                                         60
 agagangetg ggacatggat aatcacwtaa tttgctayta tyactttaat ctgactygaa
                                                                        120
 gaaccgtcta aaaataaaat ttaccatgtc dtatattcct tatagtatgc ttatttcacc
                                                                        180
 ttytttctgt ccagagagag tatcagtgac ananatttma gggtgaamac atgmattggt
                                                                        240
 gggacttnty tttacngagm accetgeeg sgegeeeteg makengantt eegesanane
                                                                        300
                                                                        301
       <210> 274
       <211>. 301
       <212> DNA
       <213> Homo sapien
       <220>
       <221> misc_feature
       <222> (1) ... (301)
       <223> n = A,T,C or G
      <400> 274
cttatatact ctttctcaga ggcaaaagag gagatgggta atgtagacaa ttctttgagg
                                                                        60
aacagtaaat gattattaga gagaangaat ggaccaagga gacagaaatt aacttgtaaa
                                                                       120
tgattctctt tggaatctga atgagatcaa gaggccagct ttagcttgtg gaaaagtcca
                                                                       180
tctaggtatg gttgcattct cgtcttcttt tctgcagtag ataatgaggt aaccgaaggc
                                                                       240
aattgtgctt cttttgataa gaagctttct tggtcatatc aggaaattcc aganaaagtc
                                                                       300
```

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301
       <210> 275
       <211> 301
       <212> DNA
       <213> Homo sapien
       <220>
       <221> misc_feature
       <222> (1)...(301)
       <223> n = A, T, C or G
       <400> 275
 tcggtgtcag cagcacgtgg cattgaacat tgcaatgtgg agcccaaacc acagaaaatg
                                                                          60
 gggtgaaatt ggccaacttt ctattaactt atgttggcaa ttttgccacc aacagtaagc
                                                                         120
 tggcccttct aataaaagaa aattgaaagg tttctcacta aacggaatta agtagtggag
                                                                         180
 tcaagagact cccaggcctc agcgtacctg cccgggcggc cgctcgaagc cgaattctgc
                                                                         240
 agatatecat cacactggeg gnegetegan catgeateta gaaggnecaa ttegecetat
                                                                         300
                                                                         301
       <210> 276
       <211> 301
       <212> DNA
       <213> Homo sapien
       <400> 276
tgtacacata ctcaataaat aaatgactgc attgtggtat tattactata ctgattatat
                                                                         60
ttatcatgtg acttctaatt agaaaatgta tccaaaagca aaacagcaga tatacaaaat
                                                                        120
taaagagaca gaagatagac attaacagat aaggcaactt atacattgag aatccaaatc
                                                                        180
caatacattt aaacatttgg gaaatgaggg ggacaaatgg aagccagatc aaatttgtgt
                                                                        240
aaaactattc agtatgtttc ccttgcttca tgtctgagaa ggctctcctt caatggggat
                                                                        300
                                                                        301
      <210> 277
      <211> 301
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc feature
      <222> (1)...(301)
      \langle 223 \rangle n = A,T,C or G
      <400> 277
tttgttgatg tcagtatttt attacttgcg ttatgagtgc tcacctggga aattctaaag
                                                                         60
atacagagga cttggaggaa gcagagcaac tgaatttaat ttaaaagaag gaaaacattg
                                                                        120
gaatcatggc actcctgata ctttcccaaa tcaacactct caatgcccca ecctcgtcct
                                                                       180
caccatagtg gggagactaa agtggccacg gatttgcctt angtgtgcag tgcgttctga
                                                                       240
gttenetgte gattacatet gaccagtete ettttteega agteentoeg tteaatettg
                                                                       300
                                                                       301
      <210> 278
      <211> 301
      <212> DNA
      <213> Homo sapien
```

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<220>
       <221> misc_feature
       <222> (1)...(301)
       \langle 223 \rangle n = A,T,C or G
       <400> 278
taccactaca ctccagcctg ggcaacagag caagacctgt ctcaaagcat aaaatggaat
                                                                         60
aacatatcaa atgaaacagg gaaaatgaag ctgacaattt atggaagcca gggcttgtca
                                                                         120
cagtetetae tgttattatg cattacetgg gaatttatat aageeettaa taataatgee
                                                                         180
aatgaacatc tcatgtgtgc tcacaatgtt ctggcactat tataagtgct tcacaggttt
                                                                         240
tatgtgttct tcgtaacttt atggantagg tactcggccg cgaacacgct aagccgaatt
                                                                         300
                                                                         301
       <210> 279
       <211> 301
       <212> DNA
       <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1) . . . (301)
      <223> n = A,T,C or G
      <400> 279
aaagcaggaa tgacaaagct tgcttttctg gtatgttcta ggtgtattgt gacttttact
                                                                         60
gttatattaa ttgccaatat aagtaaatat agattatata tgtatagtgt ttcacaaagc
                                                                        120
ttagaccttt accttccagc caccccacag tgcttgatat ttcagagtca gtcattggtt
                                                                        180
atacatgtgt agttccaaag cacataagct agaanaanaa atatttctag ggagcactac
                                                                        240
catctgtttt cacatgaaat gccacacaca tagaactcca acatcaattt cattgcacag
                                                                        300
                                                                        301
      <210> 280
      <211> 301
      <212> DNA
      <213> Homo sapien
      <400> 280°
ggtactggag ttttcctccc ctgtgaaaac gtaactactg ttgggagtga attgaggatg
                                                                         60
tagaaaggtg gtggaaccaa attgtggtca atggaaatag gagaatatgg ttctcactct
                                                                        120
tgagaaaaaa acctaagatt agcccaggta gttgcctgta acttcagttt ttctgcctgg
                                                                        180
gtttgatata gtttagggtt ggggttagat taagatctaa attacatcag gacaaagaga
                                                                        240
cagactatta actccacagt taattaagga ggtatgttcc atgtttattt gttaaagcag
                                                                       - 30.0
                                                                        301
      <210> 281
      <211> 301
      <212> DNA
      <213> Homo sapien
      <400> 281
aggtacaaga aggggaatgg gaaagagctg ctgctgtggc attgttcaac ttggatattc
                                                                         60
gccgagcaat ccaaatcctg aatgaagggg catcttctga aaaaggagat ctgaatctca
                                                                        120
atgtggtagc aatggcttta tcgggttata cggatgagaa gaactccctt tggagagaaa
                                                                        180
tgtgtagcac actgcgatta cagctaaata acccgtattt gtgtgtcatg tttgcatttc
                                                                        240
```

```
tgacaagtga aacaggatct tacgatggag ttttgtatga aaacaaagtt gcagtacctc
                                                                         300
                                                                         301
       <210> 282
       <211> 301
       <212> DNA
       <213> Homo sapien
       <400> 282
 caggtactac agaattaaaa tactgacaag caagtagttt cttggcgtgc acgaattgca
                                                                          60
 tccagaaccc aaaaattaag aaattcaaaa agacattttg tgggcacctg ctagcacaga
                                                                         120
 agcgcagaag caaagcccag gcagaaccat gctaacctta cagctcagcc tgcacagaag
                                                                         180
 cgcagaagca aagcccaggc agaaccatgc taaccttaca gctcagcctg cacagaagcg
                                                                        240
 cagaagcaaa gcccaggcag aacatgctaa ccttacagct cagcctgcac agaagcacag
                                                                        300
                                                                        301
       <210> 283
       <211> 301
       <212> DNA
       <213> Homo sapien
       <400> 283
atctgtatac ggcagacaaa ctttatarag tgtagagagg tgagcgaaag gatgcaaaag
                                                                         60
cactttgagg gctttataat aatatgctgc ttgaaaaaaa aaatgtgtag ttgatactca
                                                                        120
gtgcatctcc agacatagta aggggttgct ctgaccaatc aggtgatcat tttttctatc
                                                                        180
acttcccagg ttttatgcaa aaattttgtt aaattctata atggtgatat gcatctttta
                                                                        240
ggaaacatat acatttttaa aaatctattt tatgtaagaa ctgacagacg aatttgcttt
                                                                        300
                                                                        301
      <210> 284
      <211> 301
      <212> DNA
      <213> Homo sapien
      <400> 284
caggtacaaa acgctattaa gtggcttaga atttgaacat ttgtggtctt tatttacttt
                                                                         60
gcttcgtgtg tgggcaaagc aacatcttcc ctaaatatat attaccaaga aaagcaagaa
                                                                        120
gcagattagg tttttgacaa aacaaacagg ccaaaagggg gctgacctgg agcagagcat
                                                                        180
ggtgagaggc aaggcatgag agggcaagtt tgttgtggac agatctgtgc ctactttatt
                                                                        240
actggagtaa aagaaaacaa agttcattga tgtcgaagga tatatacagt gttagaaatt
                                                                       300
                                                                       301
      <210> 285
      <211> 301
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1) ... (301)
      <223> n = A,T,C or G
      <400> 285
acatcaccat gatcggatcc cccacccatt atacgttgta tgtttacata aatactcttc
                                                                       - 60
aatgatcatt agtgttttaa aaaaaatact gaaaactcct tctgcatccc aatctctaac
                                                                       120
```

```
caggaaagca aatgctattt acagacctgc aagccctccc tcaaacnaaa ctatttctgg
                                                                         180
 attaaatatg tetgaettet tttgaggtea caegaetagg caaatgetat ttaegatetg
                                                                         240
 caaaagctgt ttgaagagtc aaagccccca tgtgaacacg atttctggac cctgtaacag
                                                                         300
                                                                         301
       <210> 286
       <211> 301
       <212> DNA
       <213> Homo sapien
       <400> 286
taccactgca ttccagcctg ggtgacagag tgagactccg tctccaaaaa aaactttgct
                                                                         60
tgtatattat ttttgcctta cagtggatca ttctagtagg aaaggacagt aagattttt
                                                                        120
atcaaaatgt gtcatgccag taagagatgt tatattettt teteatttet teeccaceca
                                                                        180
aaaataaget accatatage trataagtet caaatttttg cettttaeta aaatgtgatt
                                                                        240
gtttctgttc attgtgtatg cttcatcacc tatattaggc aaattccatt ttttcccttg
                                                                        300.
      <210> 287
      <211> 301
      <212> DNA
      <213> Homo sapien
      <400> 287
tacagatetg ggaactaaat attaaaaatg agtgtggetg gatatatgga gaatgttggg
eccagaagga aegtagagat cagatattae aacagetttg ttttgagggt tagaaatatg
                                                                        120
aaatgatttg gttatgaacg cacagtttag gcagcagggc cagaatcctg accetetgee
                                                                        180
ccgtggttat ctcctcccca gcttggctgc ctcatgttat cacagtattc cattttgttt
                                                                        240
gttgcatgtc ttgtgaagcc atcaagattt tetegtetgt ttteetetca ttggtaatge
                                                                        300
t
                                                                        301
      <210> 288
      <211> 301
      <212> DNA
      <213> Homo sapien
      <400> 288
gtacacctaa ctgcaaggac agctgaggaa tgtaatgggc agccgctttt aaagaagtag
                                                                        60
agtcaatagg aagacaaatt ccagttccag ctcagtctgg gtatctgcaa agctgcaaaa
                                                                       120
gatetttaaa gacaatttea agagaatatt teettaaagt tggcaatttg gagateatae
                                                                       180
aaaagcatct gcttttgtga tttaatttag ctcatctggc cactggaaga atccaaacag
                                                                       240
tctgccttaa ttttggatga atgcatgatg gaaattcaat aatttagaaa gttaaaaaaa
                                                                       300
                                                                       301
      <210> 289
      <211> 301
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
     <222> (1)...(301)
     \langle 223 \rangle n = A,T,C or G
     <400> 289
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```
ggtacactgt ttccatgtta tgtttctaca cattgctacc tcagtgctcc tggaaactta
                                                                         60
 gcttttgatg tctccaagta gtccaccttc atttaactct ttgaaactgt atcatctttg
                                                                         120
 ccaagtaaga gtggtggcct atttcagctg ctttgacaaa atgactggct cctgacttaa
                                                                        180
 cgttctataa atgaatgtgc tgaagcaaag tgcccatggt ggcggcgaan aagagaaaga
                                                                        240
 tgtgttttgt tttggactct ctgtggtccc ttccaatgct gtgggtttcc aaccagngga
                                                                        300
                                                                        301
       <210> 290
       <211> 301
       <212> DNA
       <213> Homo sapien
       <220>
       <221> misc_feature
       <222> (1) ... (301).
       <223> n = A, T, C or G
       <400> 290
acactgaget ettettgata aatatacaga atgettggea tatacaagat tetatactae
                                                                         60
tgactgatct gttcatttct ctcacagctc ttacccccaa aagcttttcc accctaagtg
                                                                        120
ttctgacctc cttttctaat cacagtaggg atagaggcag anccacctac aatgaacatg
                                                                        180
gagttetate aagaggeaga aacageacag aateceagtt ttaceatteg ctageagtge
                                                                        240
tgccttgaac aaaaacattt ctccatgtct cattttcttc atgcctcaag taacagtgag
                                                                        300
                                                                        301
      <210> 291
      <211> 301
      <212> DNA
      <213> Homo sapien
      <400> 291
caggtaccaa tttcttctat cctagaaaca tttcatttta tgttgttgaa acataacaac
                                                                       60
tatatcaget agatttttt tetatgettt acetgetatg gaaaatttga cacattetge
                                                                       120
tttactcttt tgtttatagg tgaatcacaa aatgtatttt tatgtattct gtagttcaat
                                                                       180
agccatggct gtttacttca tttaatttat ttagcataaa gacattatga aaaggoctaa
                                                                       240
acatgagett caetteecca etaactaatt ageatetgtt atttettaac egtaatgeet
                                                                       300
                                                                       301
      <210> 292
      <211> 301
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(301)
      <223> n = A,T,C or G
      <400> 292
accttttagt agtaatgtct aataataaat aagaaatcaa ttttataagg tocatatagc
                                                                        60
tgtattaaat aatttttaag tttaaaaagat aaaataccat cattttaaat gttggtattc
aaaaccaaag natataaccg aaaggaaaaa cagatgagac ataaaatgat ttgcnagatg
                                                                       180
ggaaatatag tasttyatga atgttnatta aattecagtt ataatagtgg ctacacacte
                                                                       240
tcactacaca cacagacece acagteetat atgecacaaa cacattteea taaettgaaa
                                                                       300
                                                                       301
```

```
<210> 293
        <211> 301
        <212> DNA:
        <213> Homo sapien
       <400> 293
 ggtaccaagt gctggtgcca gcctgttacc tgttctcact gaaaagtctg gctaatgctc
 ttgtgtagtc acttctgatt ctgacaatca atcaatcaat ggcctagagc actgactgtt
                                                                        120
 aacacaaacg tcactagcaa agtagcaaca gctttaagtc taaatacaaa gctgttctgt
                                                                        180
 gtgagaattt tttaaaaggc tacttgtata ataacccttg tcatttttaa tgtacctcgg
                                                                        240
 ccgcgaccac gctaagccga attctgcaga tatccatcac actggcggcc gctcgagcat
                                                                        300
                                                                        301
       <210> 294
       <211> 301
       <212> DNA
       <213> Homo sapien
       <220>
       <221> misc_feature
       <222> (1)...(301)
       <223> n = A, T, C or G
       <400> 294
tgacccataa caatatacac tagctatctt tttaactgtc catcattagc accaatgaag
                                                                         60
attcaataaa attaccttta ttcacacatc tcaaaacaat tctgcaaatt cttagtgaag
                                                                        120
tttaactata gtcacaganc ttaaatattc acattgtttt ctatgtctac tgaaaataag
                                                                        180
ttcactactt ttctgggata ttctttacaa aatcttatta aaattcctgg tattatcacc
                                                                        240
cccaattata cagtagcaca accaccttat gtagttttta catgatagct ctgtagaggt
                                                                        300
                                                                        301 .
      <210> 295
      <211> 305
      <212> DNA
      <213> Homo sapien
      <400> 295
gtactctttc tctcccctcc tctgaattta attctttcaa cttgcaattt gcaaggatta
                                                                        60
cacatttcac tgtgatgtat attgtgttgc aaaaaaaaa gtgtctttgt ttaaaattac
                                                                       120
ttggtttgtg aatccatctt gctttttccc cattggaact agtcattaac ccatctctga
                                                                       180
actggtagaa aaacrtctga agagctagtc tatcagcatc tgacaggtga attggatggt
                                                                       240
totoagaaco atttoaccoa gacagootgt ttotatootg tttaataaat tagtttgggt
                                                                       300.
tctct
                                                                       305
      <210> 296
      <211> 301
      <212> DNA
      <213> Homo sapien
      <400> 296
aggtactatg ggaagctgct aaaataatat ttgatagtaa aagtatgtaa tgtgctatct
                                                                        60
cacctagtag taaactaaaa ataaactgaa actttatgga atctgaagtt attttccttg
                                                                       120
attaaataga attaataaac caatatgagg aaacatgaaa ccatgcaatc tactatcaac
                                                                       180
tttgaaaaag tgattgaacg aaccacttag ctttcagatg atgaacactg ataagtcatt
                                                                       240
```

```
tgtcattact ataaatttta aaatctgtta ataagatggc ctatagggag gaaaaagggg
                                                                          300
                                                                          301
        <210> 297
        <211> 300
        <212> DNA
        <213> Homo sapien
        <220>
        <221> misc_feature
       <222> (1)...(300)
       \langle 223 \rangle n = A,T,C or G
       <400> 297
 actgagtttt aactggacgc caagcaggca aggctggaag gttttgctct ctttgtgcta
 aaggttttga aaaccttgaa ggagaatcat tttgacaaga agtacttaag agtctagaga
                                                                         120
 acaaagangt gaaccagctg aaagctctcg ggggaanctt acatgtgttg ttaggcctgt
                                                                         180
 tccatcattg ggagtgcact ggccatccct caaaatttgt ctgggctggc ctgagtggtc
                                                                         240
 accgcacctc ggccgcgacc acgctaagcc gaattctgca gatatccatc acactggcgg
       <210> 298
       <211> 301
       <212> DNA
       <213> Homo sapien
       <220>
       <221> misc_feature
       <222> (1)...(301)
       <223> n = A,T,C or G
       <400> 298
tatggggttt gtcacccaaa agctgatgct gagaaaggcc tccctggggc ccctccegcg
                                                                        - 60
ggcatctgag agacctggtg ttccagtgtt tctggaaatg ggtcccagtg ccgccggctg
                                                                       120
tgaagetete agateaatea egggaaggge etggeggtgg tggeeacetg gaaecaceet
                                                                        180
gteetgtetg titaeattie actayeaggt titetetggg cattaenatt tgtteeceta
                                                                        240
caacagtgac ctgtgcattc tgctgtggcc tgctgtgtct gcaggtggct ctcagcgagg
                                                                        300
                                                                        301
      <210> 299
      <211> 301
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      <400> 299
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                                                                        60
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                                                                       120
tgggattgca ggctcacgcc accataccca gctaattttt ttgtattttt agtagagacg
                                                                       180
gagtttcgcc atgttggcca gctggtctca aactcctgac ctcaagcgac ctgcctgcct
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cggcctccca aagtgctgga attataggca tgagtcaaca cgcccagcct aaagatattt
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                                                                        120
 gctgcattcc acaaggttct cagcctaatg agtttcacta cctgccagtc tcaaaactta
                                                                        180
 gtaaagcaag accatgacat tcccccacgg aaatcagagt ttgccccacc gtcttgttac
                                                                        240
 tataaageet geetetaaca gteettgett etteacacea atecegageg catececcat
                                                                        300
                                                                        301
       <210> 301
       <211> 301
       <212> DNA
       <213> Homo sapien
      <400> 301
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                                                                         60
 agaggacccc aggtctccaa gcaaccacat ggtcaagggc atgaataatt aaaagttggt
                                                                        120
gggaactcac aaagaccctc agagctgaga cacccacaac agtgggagct cacaaagacc
                                                                        180
ctcagagctg agacacccac aacagtggga gctcacaaag accctcagag ctgagacacc
                                                                        240
cacaacagca cctcgttcag ctgccacatg tgtgaataag gatgcaatgt ccagaagtgt
                                                                       300
                                                                       301
       <210> 302
       <211> 301
       <212> DNA
       <213> Homo sapien
      <400> 302
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                                                                        60
tgaattttga aaattactac ttaatcctaa ttcacaataa caatggcatt aaggtttgac
                                                                       120
ttgagttggt tcttagtatt atttatggta aataggctct taccacttgc aaataactgg
                                                                       180
ccacatcatt aatgactgac ttcccagtaa ggctctctaa ggggtaagta ggaggatcca
                                                                       240
caggatttga gatgctaagg ccccagagat cgtttgatcc aaccctctta ttttcagagg
                                                                       300
                                                                       301
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      <211> 301
      <212> DNA
      <213> Homo sapien
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atattgtttt ttgacagttt aacacatctt cttctgtcag agattctttc acaatagcac
                                                                       120
tggctaatgg aactaccgct tgcatgttaa aaatggtggt ttgtgaaatg atcataggcc
                                                                       180
agtaacgggt atgttttct aactgatctt ttgctcgttc caaagggacc tcaagacttc
                                                                       240
categatttt atatetgggg tetagaaaag gagttaatet gtttteette ataaatteae
                                                                       300
                                                                       301
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   ctttttagtg tatcatatca ggaatcatct cacattggtt tgtgccatta ctggtgcagt
                                                                          120
                                                                          180
   gactttcagc cacttgggta aggtggagtt ggccatatgt ctccactgca aaattactga
                                                                          240
   ttttcctttt gtaattaata agtgtgtgtg tgaagattct ttgagatgag gtatatatct
                                                                          300
                                                                          301
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         <211> 301
         <212> DNA
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         <220>
         <221> misc_feature
         <222> (1)...(301)
         <223> n = A,T,C or G
        <400> 305
  gangtacage gtggtcaagg taacaagaag aaaaaaatgt gagtggcate etgggatgag
                                                                          60
  cagggggaca gacctggaca gacacgttgt catttgctgc tgtgggtagg aaaatgggcg
                                                                         120
  taaaggagga gaaacagata caaaatctcc aactcagtat taaggtattc tcatgcctag
                                                                         180
  aatattggta gaaacaagaa tacattcata tggcaaataa ctaaccatgg tggaacaaaa
  ttctgggatt taagttggat accaangaaa ttgtattaaa agagctgttc atggaataag
                                                                         240
                                                                         300
                                                                         301
        <210> 306
        <211> 8
        <212> PRT
        <213> Homo sapien
     <400> 306
 Val Leu Gly Trp Val Ala Glu Leu
       <210> 307
       <211> 637
       <212> DNA
       <213> Homo sapien
       <400> 307
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                                                                        120
 attgaggaat gatacttgag cccaaagagc attcaatcat tgttttattt gccttmtttt
                                                                        180
cacaccattg gtgagggagg gattaccacc ctggggttat gaagatggtt gaacacccca
                                                                        240
 cacatageac eggagatatg agateaacag tttettagee atagagatte acageecaga
                                                                        300
gcaggaggac gcttgcacac catgcaggat gacatggggg atgcgctcgg gattggtgtg
                                                                        360
aagaagcaag gactgttaga ggcaggcttt atagtaacaa gacggtgggg caaactctga
                                                                        420
tttccgtggg ggaatgtcat ggtcttgctt tactaagttt tgagactggc aggtagtgaa
                                                                        480
actcattagg ctgagaacct tgtggaatgc acttgaccca sctgatagag gaagtagcca
                                                                       540
 ggtgggagcc tttcccagtg ggtgtgggac atatctggca agattttgtg gcactcctgg
                                                                       600
 ttacagatac tggggcagca aataaaactg aatcttg
                                                                       637
       <210> 308
       <211> 647
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<212> DNA

```
<220>
       <221> misc_feature
       <222> (1)...(647)
       <223> n = A,T,C or G
       <400> 308
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 tgctcagggg aaggttcata tgggactttc tactgcccaa ggttctatac aggatataaa
                                                                        120
ggngcctcac agtatagatc tggtagcaaa gaagaagaaa caaacactga tctctttctg
                                                                        180
ccacccctct gaccctttgg aactcctctg accctttaga acaagcctac ctaatatctg
                                                                        240
ctagagaaaa gaccaacaac ggcctcaaag gatctcttac catgaaggtc tcagctaatt
                                                                        300
cttggctaag atgtgggttc cacattaggt tctgaatatg gggggaaggg tcaatttgct
                                                                       360
cattttgtgt gtggataaag tcaggatgcc caggggccag agcagggggc tgcttgcttt
                                                                        420
gggaacaatg gctgagcata taaccatagg ttatggggaa caaaacaaca tcaaagtcac
                                                                       480
tgtatcaatt gccatgaaga cttgagggac ctgaatctac cgattcatct taaggcagca
                                                                       540
ggaccagttt gagtggcaac aatgcagcag cagaatcaat ggaaacaaca gaatgattge
                                                                       600
aatgteettt tittieteet gettetgaet tgataaaagg ggaeegt
                                                                       647
      <210> 309
      <211> 460
      <212> DNA
      <213> Homo sapien
      <400> 309
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                                                                        60
aatatgattg gctgcacact tccagactga tgaatgatga acgtgatgga ctattgtatg
                                                                       120
gagcacatet teagcaagag ggggaaatae teateatttt tggccagcag ttgtttgate
                                                                       180
accaaacatc atgccagaat actcagcaaa ccttcttagc tcttgagaag tcaaagtccg
                                                                       240
ggggaattta ttcctggcaa ttttaattgg actccttatg tgagagcagc ggctacccag
                                                                       300
ctggggtggt ggagcgaacc cgtcactagt ggacatgcag tggcagagct cctggtaacc
                                                                       360
acctagagga atacacaggc acatgtgtga tgccaagcgt gacacctgta gcactcaaat
                                                                       420
ttgtcttgtt tttgtctttc ggtgtgtaag attcttaagt
                                                                       460
      <210> 310
      <211> 539
      <212> DNA
      <213> Homo sapien
      <400> 310
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ctaaaggttt taaaatatgt caggattgga agaaggcatg gataaagaac aaagttcagt
                                                                       120
taggaaagag aaacacagaa ggaagagaca caataaaagt cattatgtat tctgtgagaa
                                                                      180
gtcagacagt aagatttgtg ggaaatgggt tggtttgttg tatggtatgt attttagcaa
                                                                      240
taatetttat ggeagagaaa getaaaatee tttagettge gtgaatgate aettgetgaa
                                                                      300
ttcctcaagg taggcatgat gaaggagggt ttagaggaga cacagacaca atgaactgac
                                                                      360
ctagatagaa agccttagta tactcagcta ggaatagtga ttctgagggc acactgtgac
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atgattatgt cattacatgt atggtagtga tggggatgat aggaaggaag aacttatggc
                                                                      480
atattttcac ccccacaaaa gtcagttaaa tattgggaca ctaaccatcc aggtcaaga
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      <211> 526
     <212> DNA
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  ttttgacgtt ttctctaaac tactaaagag gcattaatga tccataaatt atattatcta
                                                                          60
  catttacago atttaaaatg tgttcagcat gaaatattag ctacagggga agctaaataa
                                                                          120
  attaaacatg gaataaagat ttgtccttaa atataatcta caagaagact ttgatatttg
                                                                         180
  tttttcacaa gtgaagcatt cttataaagt gtcataacct ttttggggaa actatgggaa
                                                                         240
  aaaatgggga aactctgaag ggttttaagt atcttacctg aagctacaga ctccataacc
                                                                         300
  tetetttaca gggageteet geageceeta cagaaatgag tggetgagat tettgattge.
                                                                         360
  acagcaagag cttctcatct aaaccctttc cctttttagt atctgtgtat caagtataaa
                                                                         420
  agttctataa actgtagtnt acttatttta atccccaaag cacagt
                                                                         480
                                                                         526
        <210> 312
        <211> 500
        <212> DNA
       <213> Homo sapien
       <220> .
       <221> misc_feature
       <222> (1) ... (500)
       <223> n = A,T,C \text{ or } G
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 tcatttctga aagcagttga gccactttat tccaaagtac actgcagatg ttcaaactct
 ccatttetet ttecetteca cetgecagtt ttgctgacte tcaacttgte atgagtgtaa
                                                                        120
 gcattaagga cattatgctt cttcgattct gaagacaggc cctgctcatg gatgactctg
                                                                        180
 gcttcttagg aaaatatttt tcttccaaaa tcagtaggaa atctaaactt atcccctctt
                                                                        240
 tgcagatgtc tagcagcttc agacatttgg ttaagaaccc atgggaaaaa aaaaaatcct
                                                                        300
 tgctaatgtg gtttcctttg taaaccanga ttcttatttg nctggtatag aatatcaget
                                                                        360
ctgaacgtgt ggtaaagatt tttgtgtttg aatataggag aaatcagttt gctgaaaagt
                                                                        420
                                                                        480
tagtcttaat tatctattgg
                                                                        500
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       <211> 718
       <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
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      <223> n = A,T,C or G
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tgatgataca gaggtgagaa ataagaaagg ctgctgactt taccatctga ggccacacat
                                                                        60
ctgctgaaat ggagataatt aacatcacta gaaacagcaa gatgacaata taatgtctaa
                                                                       120
gtagtgacat gtttttgcac atttccagcc cttttaaata tccacacaca caggaagcac
                                                                       180
aaaaggaagc acagagatcc ctgggagaaa tgcccggccg ccatcttggg tcatcgatga
                                                                       240
geetegeeet gtgeetgnte eegettgtga gggaaggaea ttagaaaatg aattgatgtg
                                                                       300
tteettaaag gatggeagga aaacagatee tgttgtggat atttatttga aegggattae
                                                                       360
                                                                       420
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<212> DNA

106

agatttgaaa tgaagtcaca aagtgagcat taccaatgag aggaaaacag acgagaaaat	480
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aactggggag gagataccac ggggcagagg tcaggattct ggccctgctg cctaactgtg	600
cgttatacca atcatttcta tttctaccct caaacaagct gtngaatatc tgacttacgg	660
ttettntgge ceacatttte atnateeace cententtt aannttante caaantgt	
and a second outlined outlined	718
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caacatgtgt agatetettg tettattett ttgtetataa taetgtattg tgtagtecaa	120
gctctcggta gtccagccac tgtgaaacat gctcccttta gattaacctc gtggacgctc	180
ttgttgtatt gctgaactgt agtgccctgt attttgcttc tgtctgtgaa ttctgttgct	240
totaggacat troottatas tacagaggas caccagaggas atmosphase	300
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<211> 341	
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(213) NOINO BAPTEN	
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•	
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gacccccatt ctgaagatgt ctggaacctc taccagcagg atgatgatag ccccaatgac	180
agtcaccage teceegacca geeggatate gteettaggg gteatgtagg etteetgaag	240
tagcttctgc tgtaagaggg tgttgtcccg ggggctcgtg cggttattgg tcctgggctt	30,0
gagggggggg tagatgcagc acatggtgaa gcagatgatg t	341
.010. 010	
<210> 316	
<211> 151	***
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<213> Homo sapien	
<400> 316	
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tgtgggcctt tctcgagttt ctgattataa acaccactgg agcgatgtgt tgactggact	120
cattcaggga gctctggttg caatattagt t	151
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<211> 151	
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AtCttCattt atCtCtCCCC ttasacctcc ctcctcccc	60 120
ccagggctct gttcttgcca cacctgcttg a	120
	151
<210> 318	• •
<211> 151	•

### 107

<213> Homo sapien <400> 318 actggtggga ggcgctgttt agttggctgt tttcagaggg gtctttcgga gggacctcct 60 gctgcaggct ggagtgtctt tattcctggc gggagaccgc acattccact gctgaggctg 120 tgggggggt ttatcaggca gtgataaaca t 151 . <210> 319 <211> 151 <212> DNA <213> Homo sapien <400> 319 aactagtgga tecagageta taggtacagt gtgateteag etttgcaaac acattteta 60 catagatagt actaggtatt aatagatatg taaagaaaga aatcacacca ttaataatgg 120 taagattggg tttatgtgat tttagtgggt a 151 <210> 320 <211> 150 <212> DNA <213> Homo sapien <400> 320 aactagtgga tecaetagte cagtgtggtg gaattecatt gtgttggggt tetagatege gageggetge cettttttt ttttttttg ggggggaatt tttttttt aatagttatt 120 gagtgttcta cagcttacag taaataccat <210> 321 <211> 151 <212> DNA <213> Homo sapien <400> 321 agcaactttg tttttcatcc aggttatttt aggcttagga tttcctctca cactgcagtt 60 tagggtggca ttgtaaccag ctatggcata ggtgttaacc aaaggctgag taaacatggg 120 tgcctctgag aaatcaaagt cttcatacac t 151. <210> 322 <211> 151 <212> DNA <213> Homo sapien <220> <221> misc\_feature <222> (1) . . . (151) <223> n = A, T, C or G<400> 322 atccagcate ttetectgtt tettgeette ettttette ttettasatt etgettgagg 60 tttgggcttg gtcagtttgc cacagggctt ggagatggtg acagtcttct ggcattcggc 120 attgtgcagg gctcgcttca nacttccagt t

<210> 323 <211> 151 <212> DNA

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<213> Homo sapien
        <220>
        <221> misc_feature
        <222> (1)...(151)
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 nagactcant tactacccag tttgtggttt twtgggagaa atgtaactgg acagttagct
                                                                          60
                                                                         120
  gttcaatyaa aaagacactt ancccatgtg g
                                                                         151
        <210> 324
        <211> 461
        <212> DNA
        <213> Homo sapien
        <220>
       <221> misc_feature
       <222> (1)...(461)
       <223> n = A,T,C or G
       <400> 324
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                                                                         60 .
 agaagtggtc agctaaagga atccaggttg ttggttggac tgttaatacc tttgatgaaa
                                                                        120
 agagttacta cgaatcccat cttggttcca gctatatcac tgacagcatg gtagaagact
                                                                        180
 gcgaacctca cttctagact ttcacggtgg gacgaaacgg gttcagaaac tgccaggggc
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 ctcatacagg gatatcaaaa taccctttgt gctacccagg ccctggggaa tcaggtgact
                                                                        300.
 cacacaaatg caatagttgg tcactgcatt tttacctgaa ccaaagctaa acccggtgtt
                                                                        360
 gccaccatgc accatggcat gccagagttc aacactgttg ctcttgaaaa ttgggtctga
                                                                        420
 aaaaacgcac aagagcccct gccctgccct agctgangca c
                                                                        461
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       <211> 400
      <212> DNA
       <213> Homo sapien
       <400> 325
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                                                                         60
tttgatgtct ccaagtagtc caccttcatt taactctttg aaactgtatc atctttgcca
                                                                        120
agtaagagtg gtggcctatt tcagctgctt tgacaaaatg actggctcct gacttaacgt
                                                                        180
tctataaatg aatgtgctga agcaaagtgc ccatggtggc ggcgaagaag agaaagatgt
                                                                        240
gttttgtttt ggactctctg tggtcccttc caatgctgtg ggtttccaac caggggaagg
                                                                        300
gtcccttttg cattgccaag tgccataacc atgagcacta cgctaccatg gttctgcctc
                                                                        360
ctggccaagc aggctggttt gcaagaatga aatgaatgat
                                                                        400
      <210> 326
      <211> 1215
      <212> DNA
      <213> Homo sapien
      <400> 326
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gttctgctcg ggcgtcctgg tgcatccgca gtgggtgctg tcagccgcac actgtttcca
                                                                       120
gaacteetae accateggge tgggeetgea cagtettgag geegaceaag ageeagggag
                                                                       180
```

```
ccagatggtg gaggccagec tetecgtacg geacccagag tacaacagac cettgetege
                                                                   240
taacgacctc atgctcatca agttggacga atccgtgtcc gagtctgaca ccatccggag
                                                                   300
catcagcatt gcttcgcagt gccctaccgc ggggaactct tgcctcgttt ctggctgggg
                                                                   360
tetgetggcg aacggcagaa tgcctaccgt gctgcagtgc gtgaacgtgt cggtggtgtc
                                                                   420
tgaggaggtc tgcagtaagc tctatgaccc gctgtaccac cccagcatgt tctgcgcegg
                                                                   480
cggagggcaa gaccagaagg actcctgcaa cggtgactct ggggggcccc tgatctgcaa
                                                                   540
cgggtacttg cagggccttg tgtctttcgg aaaagccccg tgtggccaag ttggcgtgcc
                                                                   600
aggtgtctac accaacctct gcaaattcac tgagtggata gagaaaaccg tccaggccag
                                                                   660
ttaactctgg ggactgggaa cccatgaaat tgacccccaa atacatcctg cggaaggaat
                                                                   720
tcaggaatat ctgttcccag cccctcctcc ctcaggccca ggagtccagg cccccagccc
                                                                   780
ctectecete aaaccaaggg tacagatece cageceetee teeteagae ccaggagtee
                                                                   840
agacececca geceetecte ceteagacee aggagtecag eccetectee eteagaceea
                                                                   900
ggagtccaga cccccagcc cctcctcct cagacccagg ggtccaggcc cccaacccct
                                                                  960
cctccctcag actcagaggt ccaagccccc aacccctcct tccccagacc cagaggtcca
                                                                  1020
ggteccagec cetecteet cagacccage ggtecaatge cacetagaet etecetgtae
                                                                 1080
acagtgcccc cttgtggcac gttgacccaa ccttaccagt tggtttttca tttttgtcc
                                                                 1140
1200
aaaaaaaaa aaaaa
                                                                 1215
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<211> 220

<212> PRT

<213> Homo sapien

<400> 327

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<212> PRT

<213> Homo sapien

#### <400> 336

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 Phe
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 Thr
 Leu
 Leu
 Ser
 Arg
 Arg
 His
 Leu
 Gly
 Ser
 Tyr
 Leu

 Leu
 Asp
 Ser
 Glu
 Asn
 Thr
 Ser
 Gly
 Ala
 Leu
 Pro
 Arg
 Leu
 Pro
 Arg
 Leu
 Pro
 Arg
 Leu
 Pro
 Arg
 Leu
 Arg
 Ala
 Ala
 Ala
 Phe
 Ser
 His
 Gln
 Lys
 Pro
 Gln
 Lys
 Pro
 Ala
 Leu
 Ser
 Ala
 Ala
 Leu
 Thr
 Gln
 Thr
 Gln
 Gln
 Ala
 Ala
 Ala
 Ala
 Leu
 Thr
 Gln
 Thr
 Gln
 Blue
 Ala
 Ala
 Ala
 Leu
 Thr
 Gln
 Ala
 Ala
 Ala
 Leu
 Thr
 Gln
 Ala
 Ala

```
      Val
      Lys
      Ile
      Trp
      Phe
      Gln
      Asn
      Arg
      Arg
      Tyr
      Lys
      Thr
      Lys
      Arg
      Lys
      Gln
      90
      95

      Leu
      Ser
      Ser
      Glu
      Leu
      Gly
      Asp
      Leu
      Glu
      Lys
      His
      Ser
      Ser
      Leu
      Pro
      Ala

      Leu
      Lys
      Glu
      Glu
      Ala
      Phe
      Ser
      Arg
      Ala
      Ser
      Leu
      Val
      Ser
      Val
      Tyr
      Asn

      115
      120
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      125
      125
      125
      125
      125
      126
      140

      Ala
      Phe
      Trp
      Tyr
      Pro
      Tyr
      Leu
      Tyr
      Cys
      Val
      Gly
      Ser
      Trp
      Ser
      Pro

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<213> Homo sapien

<400> 337

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<210> 338

<211> 9

<212> PRT

<213> Homo sapien

<400> 338

Leu Leu Ala Asn Asp Leu Met Leu Ile 1 5

<210> 339

<211> 318

<212> PRT

<213> Homo sapien

<400> 339s

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				102					170					100		
Ser	Leu	Ala	HIS	His	Leu	Gly	Arg	Ile	His	Phe	His	Asn	Leu	Gln	Gly	
			190					185					100		_	
Giu	nys	195	ıyr	ASN	Ala	GIY	Leu	Ala	Tyr	Cys	His	Ser	Lys	Leu	Ala	
Agn	Tia		Dho	Th-	Ø1 =	~1	200		_			205			-	
74311	210	Leu	File	IIIL	GIN	GIU	Leu	Ala	Arg	Arg	Leu	Lys	Gly	Ser	Gly	
Val		Thr	Tree	Sar	17-3	215	Dwa	<b>~</b> 3	<b></b>		220					
225	****	****	-y_	361	230	urs	PIO	GIY	Inr	val	Gln	Ser	Glu	Leu	Val	
_	His	Ser	Ser	Dhe		λ~~	~	Mak		235	_				240	
5			JUL	245	Mec	ALG	пр	Met	Trp	Trp	Leu	Phe	Ser		Phe	
Ile	Lvs	Thr	Pro		Gln	Gly	772	Gln.	250	C			Cys	255		
			260	<b></b>	<b>U</b>	CLY	nia	265	THE	ser	ren	His		Ala	Leu	-
Thr	Glu	Glv		Glu	Ile	T.eu	Ser	G1v	Nan	ui.	Dh.	<b>^</b>	270 Asp	_		
		275				acu.	280	Gry	ASII	uis	rne		Asp	Cys	His	
Val	Ala	Trp	Val	Ser	Ala	Gln	Ala	Ara	Aen	G3.,	Th-	285	Ala			
	290	•				295		9	AQII	Gru	300	TTE	ATA	Arg	Arg	
Leu	Trp	Asp	Val	Ser	Cys		Leu	Leu	Glv	Len	Dro	T10	2			
305					310					315	110	116	Asp			
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		10>									٠.				• •	
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•		12>														
	<2	13>	Homo	sap	ien							٠.				
•				•				•	·					•	•	
		00>														
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cgga	cacci	99 6	yyya	ggcg	c tg	cctad	acca	acto	attti	tca (	Jagge	70+0				120
CCCC	Lyce	yc a	gyct	Jgagı	c gco	CCCC	BEEC	ctad	rcaac	rag :	accad	7202	++ ~			180
9900	3-35	99 Y	Jygu	LEAL	: agg	gcagt	cqat	aaaa	cataa	aga 1	ates	3+++		-~		240
	-aati		JUCL	Legge	: tga	acqac	caaa	atco	atac	ita i	CCCC	72 to				300
9000	-aaai	-y cy	jacai	Caci	: gat	gcto	בככ	tcac	raaat	ac t	cate	1000	-~ ~*			360
- Sec	-aac		juual	.ccya	ı CEC	בכםכ	CCC	aaac	:tata	ita s	anac	2001	-~			420
ctg		י בנ	.ccaç	jaatt	. caa	iagto	jaaa	ggca	gcac	cc c	taag	ctc	g ac	tccg	atge jatge	480
ccg				•									•			483
٠.	~ Ž1	.0> 3	111						,				4	•		
		.1> 3					•				٠			.*		
		.2> D								• )		, ••				
			lomo	gani												
				adhi	CII											
	<40	0> 3	41													
ctact				gatt	+00	ttat	222									: .
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tattt	ctta	C 99	gtat	tass	tat	ttts	aya -	aaid	getg:	ag a	gcct	ctaa	a cc	aact	ctct	120
gctgc	ttta	a ta	attt	cuaa ctr=	tac	tare	 	2+	.cat	aa a	gagt	agct	c aa	aata	tgca	180
attaa	actr	a at	gaaa.	aact	cya	-33r	202	= LCC(	ycag!	ca a	catg	tata	t ca	tcta	ttag	240
aattt. ctgat	terr	a ac	atto	tott	tas	tasa	cac ·	aadti	Lugua	aa C	cacta	agca	C tta	aagt	actc	300
- 30			9		caa	cyaci	Lac (	aaya	.aac(	ca a	cag					344
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                                                                         120
 cctggcaggt aaaccaatgc caagagagtg atggaaacca ttggcaagac tttgttgatg
                                                                        180
 accaggattg gaattttata aaaatattgt tgatgggaag ttgctaaagg gtgaattact
                                                                        240
 teceteagaa gagtgtaaag aaaagteaga gatgetataa tageagetat tttaattgge
                                                                        300
 aagtgccact gtggaaagag ttcctgtgtg tgctgaagtt ctgaagggca gtcaaattca
                                                                        360
 tcagcatggg ctgtttggtg caaatgcaaa agcacaggtc tttttagcat gctggtctct
                                                                        420
 cccgtgtcct tatgcaaata atcgtcttct tctaaatttc tcctaggctt cattttccaa
                                                                        480
 agttettett ggtttgtgat gtettttetg ettteeatta attetataaa atagtatgge
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       <211> 382
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                                                                        120
cttgtaactc tcctttctcc tttcttcccc tttctctgcc cgcctttccc atcctgctgt
                                                                        180
agacttettg attgtcagte tgtgtcacat ceagtgattg ttttggttte tgttccettt
                                                                        240
ctgactgccc aaggggctca gaaccccagc aatcccttcc trtcactacc trctttttg
                                                                        300
ggggtagttg gaagggactg aaattgtggg gggaaggtag gaggcacatc aataaagagg
                                                                        360
aaaccaccaa gctgaaaaaa aa
                                                                        382
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      <211> 536
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                                                                       120
gtttaggggg atgccaagga taaggccagc tcagttatat gaagagaagc agaacaaaca
                                                                       180
agtettteag agaaatggat geaateagag tgggateeeg gteacateaa ggteacaete
                                                                       240
caccttcatg tgcctgaatg gttgccaggt cagaaaaatc cacccttac gagtgcggct
                                                                       300
togaccotat atcoccogco ogogtocott totocataaa attottotta gtagotatta
                                                                       360
ccttcttatt atttgatcta gaaattgccc tccttttacc cctaccatga gccctacaaa
                                                                       420
caactaacct gccactaata gttatgtcat ccctcttatt aatcatcatc ctagccctaa
                                                                       480
gtctggccta tgagtgacta caaaaaggat tagactgagc cgaataacaa aaaaaa
                                                                       536
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      <211> 251
      <212> DNA
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tgaatgaage ecceatettt gtgeeteetg aaaagagagt ggaagtgtee gaggaetttg
                                                                       120
gcgtgggcca ggaaatcaca tcctacactg cccaggagcc agacacattt atggaacaga
                                                                       180
aaataacata teggattigg agagacaetg ceaactgget ggagattaat eeggacaetg
                                                                       240
gtgccatttc c
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  ctaagtettg ttaccaaaaa aaggaaaaag aaaagatett eteagttaca aattetggga
  agggagacta tacctggctc ttgccctaag tgagaggtct tccctcccgc accaaaaaat
                                                                         120
  agaaaggett tetattteae tggeecaggt agggggaagg agagtaaett tgagtetgtg
                                                                         180
                                                                         240
  ggtctcattt cccaaggtgc cttcaatgct catnaaaacc aa
                                                                         282
        <210> 347
        <211> 201
       <212> DNA
        <213> Homo sapien
       <220>
       <221> misc_feature
       <222> (1) ... (201)
       <223> n = A,T,C or G
       <400> 347
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 taaatataac ttttaaaana ntactancag cttttaccta ngctcctaaa tgcttgtaaa
                                                                         60
 tetgagaetg aetggaecea eecagaecea gggeaaagat acatgttace atateatett
                                                                        120
                                                                        180
 tataaagaat tttttttgt c
       <210> 348
       <211> 251
       <212> DNA
       <213> Homo sapien
       <400> 348
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agagagaaca gtgccagaat gaaactgacc ctaagtccca ggtgcccctg ggcaggcaga
aggagacact cccagcatgg aggagggttt atcttttcat cctaggtcag gtctacaatg
                                                                        120
                                                                        180
ggggaaggtt ttattataga acteceaaca geceaectea etectgeeae ecaeecgatg
                                                                        240
gccctgcctc c
                                                                        251
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aacccctgag gatgccagag ctatgggtcc agaacatggt gtggtattat caacagagtt
                                                                        60
cagaagggtc tgaactctac gtgttaccag agaacataat gcaattcatg cattccactt
                                                                       120
agcaattttg taaaatacca gaaacagacc ccaagagtct ttcaagatga ggaaaattca
                                                                       180
                                                                       240
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actcctggtt t

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251
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  agecegeeeg gtgaageteg etgettteee taceteetta agtgaetgee aaaegeeeae
                                                                          60
 cggctggaat tgctctggtt atgatgacag agaaaatgat ctcttcctct gtgacaccaa
                                                                         120
 cacctgtaaa tttgatgggg aatgtttaag aattggagac actgtgactt gcgtctgtca
                                                                         180
 gttcaagtgc aacaatgact atgtgcctgt gtgtggctcc aatggggaga gctaccagaa
                                                                         240
 tgagtgttac ctgcgacagg ctgcatgcaa acagcagagt gagatacttg tggtgtcaga
                                                                         300
 aggatcatgt gccacagtcc atgaaggctc tggagaaact agtcaaaagg agacatccac
                                                                         360
                                                                         420
 ctgtgatatt tgccagtttg gtgcagaatg tgacgaagat gccgaggatg tctggtgtgt
 gtgtaatatt gactgttctc aaaccaactt caatcccctc tgcgcttctg atgggaaatc
                                                                         480
 ttatgataat gcatgccaaa tcaaagaagc atcgtgtcag aaacaggaga aaattgaagt
                                                                         540
 catgicititg ggicgatgic aagataacac aactacaact actaagictg aagatgggca
                                                                        600
 ttatgcaaga acagattatg cagagaatgc taacaaatta gaagaaagtg ccagagaaca
                                                                        660
 ccacatacct tgtccggaac attacaatgg cttctgcatg catgggaagt gtgagcattc
                                                                        720
 tatcaatatg caggagccat cttgcaggtg tgatgctggt tatactggac aacactgtga
                                                                        780
 aaaaaaggac tacagtgttc tatacgttgt teceggteet gtacgattte agtatgtett
                                                                        840
                                                                        900
 aatcgcag
                                                                        908.
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gtcaaacctt aatgccattg ttattgtgaa ttaggattaa gtagtaattt tcaaaattca
cattaacttg attttaaaat cagwtttgyg agtcatttac cacaagctaa atgtgtacac
tatgataaaa acaaccattg tattcctgtt tttctaaaca gtcctaattt ctaacactgt
                                                                        180
atatateett egacateaat gaaetttgtt ttettttaet eeagtaataa agtaggeaca
                                                                        240
                                                                       300
gatctgtcca caacaaactt gcctctcat gccttgcctc tcaccatgct ctgctccagg
tragerert titiggerigt tigttitgte aaaaacetaa tetgetiett getettettg
                                                                       360
                                                                       420
gtaatatata tttagggaag atgttgcttt gcccacacac gaagcaaagt aa
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tgtggataag gccaggtcaa tggctgcaag catgcagaga aagaggtaca tcggagcgtg
                                                                      60
                                                                       120
caggetgegt teegteetta egatgaagae caegatgeag tttecaaaca ttgocactae
                                                                      180
atacatggaa aggaggggga agccaaccca gaaatgggct ttctctaatc ctgggatacc
                                                                      240
aataagcaca a
                                                                      251
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<212> DNA

# <213> Homo sapien

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gtatccaaaa gcaaaacagc agatatacaa aattaaagag acagaagata gacattaaca	180
gataaggcaa cttatacatt gacaatccaa atccaataca tttaaacatt tgggaaatga	240
gggggacaaa tggaagccar atcaaatttg tttaaaacta ttcagtatgt ttcccttgct	300
teatgetga raaggetete cetteatgg ggatgacaaa etecagatge teceetiget	360
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	436
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Superior Superior	
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ctggcagtag aagctgttct ccaggtacat ttctctagct catgtacaaa aacatcctga	180
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aggactttgt caggtgcctt gctaaaagcc agatgcgttc ggcacttcct tggtctgagg ttaattgcac acctacaggc actgggctca tgctttcaag tattttgtcc tcactttagg	300
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gagtacatgc agtaatgggg tagatgtgtg tggtgtgtct tcattcctgc aagggtgctt	420
gttagggagt gtttccagga ggaacaagtc tgaaaccaat catgaaataa atggtaggtg	480
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caatatggaa ggetetaatt tgeecatatt tgaaataata atteagettt ttgtaataca	600
aaataacaa ggattgagaa tcatggtgtc taatgtataa aagacccagg aaacataaat	660
atatcaactg cataaatgta aaatgcatgt gacccaagaa ggccccaagg aaacataaat	720
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TODOUTED TODOUTED ENDADING COARCASTALLE	60
The state of the s	120
gacagcateg etgtaaaaag cetaceaatg agageteagt teaaggegaa ceacecette	180
	240
TOTAL TOTAL ACTION OF A CONTRACT CONTRA	300
gtgactttcc cacggccaaa aagctgttca cacttcacgc acctctgtgc ctcagtttgc	360
tcatctgcaa aataggtcta ggatttcttc caaccatttc atgagttgtg aagctaaggc	420
tttgttaatc atggaaaaag gtagacttat gcagaaagcc tttctggctt tcttatctgt	480
ggtgtctcat ttgagtgctg tccagtgaca tgatcaagtc aatgagtaaa attttaaggg	540
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<211> 574

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                                                                      120
 caagetteee atttgtagat etcagtgeet atgagtatet gacacetgtt ectetetea
                                                                      180
 gtctcttagg gaggcttaaa tctgtctcag gtgtgctaag agtgccagcc caaggkggtc
                                                                      240
 aaaagtccac aaaactgcag tetttgetgg gatagtaage caagcagtge etggacagca
                                                                      300
 gagttetttt ettgggeaac agataaccag acaggaetet aategtgete ttatteaaca
                                                                      360
 ttettetgte tetgeetaga etggaataaa aageeaatet etetegtgge acagggaagg
                                                                      420
 480
 gatagacggc acagggagct cttaggtcag cgctgctggt tggaggacat tcctgagtcc
                                                                     540
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      <213> Homo sapien
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                                                                     120
aagccacaac caaracttga ttttatcaac aaaaacccct aaatataaac ggsaaaaaag
                                                                     180
atagatataa ttattccagt ttttttaaaa cttaaaarat attccattgc cgaattaara
                                                                     240
araarataag tgttatatgg aaagaagggc attcaagcac actaaaraaa cctgaggkaa
                                                                     300
gcataatctg tacaaaatta aactgtcctt tttggcattt taacaaattt gcaacgktct
                                                                     360
ttttttttt tttctgtttt tttttttt tac
                                                                     393
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      <211> 630
      <212> DNA
      <213> Homo sapien
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                                                                    120
gcatagagta gggaagctaa tccagcacag ggaggtcaca gagacatccc taaggaagtg
                                                                    180
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agattettag t	
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- 33 - 44 AND STOCK GRANGELLEGIC LEGIC FOR CHARACTER	300
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o o o o o o o o o o o o o o o o o o o	120
The state of the s	180
The state of the s	240
J-J-J-J-J-J-J-J-J-J-J-J-J-J-J-J-J-J-J-	300
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	- 333	· uyaaacauc	a Lacterero	7 CCAtatta.		240
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	- 3-3-3-6-6-6-6	- Cullalal	C CAECCAACA	~ эгггэээ		360
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<212> DNA

<213> Homo sapien

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2184

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480

540

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	50		/ Gln			55					60				_
65			J Leu		70					75					8:0
			Leu	85					90			~		95	•
			Gly 100					105					110		٠-,
		115				•	120					125		_	
	130		Pro			135					140	Arg	Asp		
145			Arg		150					155		٠			160
			Asn	165	•		•		170					175	Cys
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Gly	Ala	Asp	Ile	Glu 245	Ser	Lys	Asn	Lys	His 250	Gly	Leu	Thr	Pro	Leu 255	Leu
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Lys	Lys	Ala 275	Asn	Leu	Asn	Ala	Leu 280	Asp	Arg	Tyr	Gly	Arg 285	Thr	Ala	Leu
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Gln Lys Arg Thr Ala Leu His Leu Ala Ser Ala Asn Gly Asn Ser Glu
  50 55 60
Val Val Lys Leu Xaa Leu Asp Arg Arg Cys Gln Leu Asn Val Leu Asp
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Asn Lys Lys Arg Thr Ala Leu Xaa Lys Ala Val Gln Cys Gln Glu Asp
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            85
Glu Cys Ala Leu Met Leu Leu Glu His Gly Thr Asp Pro Asn Ile Pro
         100 105
Asp Glu Tyr Gly Asn Thr Thr Leu His Tyr Ala Xaa Tyr Asn Glu Asp
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His Asp Asp Ser Ala Met Lys Thr Leu Arg Ser Lys Met Gly Lys Trp
Cys Arg His Cys Phe Pro Cys Cys Arg Gly Ser Gly Lys Ser Asn Val
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Gly Ala Ser Gly Asp His Asp Asp Ser Ala Met Lys Thr Leu Arg Asn

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		11!	5			•	120	)				12	p Sei 5	Al.	-
Met	: Glu 130	ı Pro	Arg	у Туз	. His	Va]		g Gly	Glu	ı Ası	Let 140		p Lys	Le	u Hi
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				165	5				170	)			s Arg	179	r Ala
			180	)				185				•	l Lys 190	Let	Lei
	•	195	j				200	)				209	Lys	Arg	
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Pro 385	Arg	Thr	His	Met	<b>V</b> al	Val	Glu	Val	Asp	Ser 395	Met	Pro	Ala	Ala	Ser
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ľhr	Ser	Gly 435	Asp	His	Asp	Asp	Ser .		Met .	Lys	Thr-	Leu 445	Arg	Ser	Lys
let	Gly 450	Lys	Trp	Cys	Arg	His 455	Cys	Phe	Pro		Cys 460	Arg	Gly	Ser	Gly
ys 165	Ser	Asn	Val	Gly				Asp				Ser	Ala	Met	
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Leu	Ile	Val	Met	Leu	. Arg	Asp	Thr	Asp	Val	Asr	Lvs	Lvs	a Ası	Lvi	Gln	1
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126	5				1270	i				1275	5		Thr		128
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		1395					1400					1405		u٢	TYL

_		_			_	_		_	_						
Lys				Met	Leu			Ser	Ser	Glu			Asn	Pro	Glu
0.		0			4	141	-				142				
		Leu	Lys	Leu			Glu	Glu	Glu	Ser		Arg	Phe	Lys	Gly
142		•			143	-				143					144
Ser	Glu	Asn	Ser	Gln	Pro	Glu	Lys	Met		Gļn	Glu	Pro	Glu	Ile	Asr
		•	· .	144	_				145					145	
Lys	Asp	Gly	Asp	Arg	Glu	Val	Glu	Glu	Glu	Met	Lys	Lys	His	Glu	Ser
			146					146					147		•
Asn	Asn	Val	Gly	Leu	Leu	Glu	Asn	Leu	Thr	Asn	Gly	Val	Thr	Ala	Gly
		147					148				•	148			-
Asn	Gly	Asp	Asn	Gly	Leu	Ile	Pro	Gln	Arg	Lys	Ser	Arg	Thr	Pro	G1u
	149					149					150				
Asn	Gln	Gln	Phe	Pro	Asp	Asn	Glu	Ser	Glu	Glu	Tyr	His	Arg	Ile	Cys
150	5 .				151	0				151	5	•			152
Glu	Leu	Val	Ser	Asp	Tyr	Lys	Glu	Lys	Gln	Met	Pro	Lys	Tyr	Ser	Ser
				152	5 .	_		_	153	0		• •	•	153	5
Glu	Asn	Ser	Asn	Pro	Glu	Gln	Asp	Leu	Lys	Leu	Thr	Ser	Glu	Glu	Glu
			154		• •		_	154					155		,-
Ser	Gln	Arg	Leu	Glu	Gly	Ser	Glu	Asn	Gly	Gln	Pro	Glu	Lys	Arq	Ser
		155					156					156		_	
Gln	Glu	Pro	Glu	Ile	Asn	Lys	Asp	Gly	Asp	Arg	Glu	Leu	Glu	Asn	Phe
	157	0			,	157	5	_		: <b>-</b>	158	0		*	
Met	Ala	Ile	Glu	Glu	Met	Lys	Lys	His	Gly	Ser	Thr	His	Val	Gly	Phe
1589	-		•		159	) .		٠.		1595					160
Pro	Glu	Asn	Leu	Thr	Asn	Gly	Ala	Thr	Ala	Gly	Asn	Gly	Asp	Asp	Gly
				1609	5.		100	•		)				161	
Leu	Ile	Pro	Pro	Arg	Lys	Ser	Arg	Thr	Pro	Glu	Ser	Gln	Gln	Phe	Pro
		• •	1620	•			٠.	1629	5	• •	•		1630	<u>ַ</u>	
Asp	Thr	Glu	Asn	Glu	Glu	Tyr	His	Ser	Asp	Glu	Gln	Asn	Asp	Thr	Gln
		1639	5				1640	)			·	1645	5		
Lys	Gln	Phe	Cys	Glu	Glu	Gln	Asn	Thr	Gly	Ile	Leu	His	Asp	Glu	Ile
	1650	)	21			165	5	•			1660		_		•
Leu	Ile	His	Glu	Glu	Lys	Gln	Ile	Glu	Val	Val	Glu	Lys	Met	Asn	Ser
1665			• •		1670	). `	•			1675		-			168
Glu	Leu	Ser	Leu	Ser	Cys	Lys	Lys	Glu	Lys	Asp	Ile	Leu	His	Glu	Asn
			3	1685						):				1695	
Ser	Thr	Leu	Arg	Glu	Glu	Ile	Ala	Met	Leu	Arg	Leu	Glu	Leu	Asp	Thr
			1700	) '				1705					1710		٠.
Met	Lys	His	Gln												
	_	1715											•		
				•											
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<211> 656

<212> PRT

<213> Homo sapien

<400> 379

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65					70					75					n <b>V</b> a:
				85					- 90					. 95	g Ası
			100	0				10	5				141	g G1	y Ser
		11:	•				120	)				12	p Se:	r Al	a Phe
	130	)				135	5.				140	)			u His
145					150	)				155	5				l Met
			•	165	5				170	)				179	r Ala
			- 180	)	•			185	5				190	ì	Leu
		195					200				•	205	5		Thr
	210					215	;				220				Met
225					230					235					Asn 240
				245					250					255	Lys
			260					265					270		Gly
		275					280					285			Val
	290				Lys	295					300				
305	•				310					315					Ile 320
				325					330				•	335	Leu
			340		Arg			345					350		
		355			Ser		360					365			
	370				Asn	375					380				
385					390					395					Lys
				405	Glu				410					415	
			420		His			425					430		
		435			Thr		440					445			
	450					455					460				
465					Arg 470					475					480
				485	Tyr				490		•			495	_
	~y .5		****	GCT	GIU '	GIU	GTÜ	oer	GTU	Arg	ren	Glu	Gly	Ser	Glu

505 Asn Gly Gln Pro Glu Leu Glu Asn Phe Met Ala Ile Glu Glu Met Lys 520 Lys His Gly Ser Thr His Val Gly Phe Pro Glu Asn Leu Thr Asn Gly 535 Ala Thr Ala Gly Asn Gly Asp Asp Gly Leu Ile Pro Pro Arg Lys Ser 550 555 Arg Thr Pro Glu Ser Gln Gln Phe Pro Asp Thr Glu Asn Glu Glu Tyr 570 His Ser Asp Glu Gln Asn Asp Thr Gln Lys Gln Phe Cys Glu Glu Gln 580 585 Asn Thr Gly Ile Leu His Asp Glu Ile Leu Ile His Glu Glu Lys Gln 600 Ile Glu Val Val Glu Lys Met Asn Ser Glu Leu Ser Leu Ser Cys Lys 615 620 Lys Glu Lys Asp Ile Leu His Glu Asn Ser Thr Leu Arg Glu Glu Ile 630 635 Ala Met Leu Arg Leu Glu Leu Asp Thr Met Lys His Gln Ser Gln Leu 645 650°

<210> 380

<211> 671

<212> PRT

<213> Homo sapien

<400> 380

Met Val Val Glu Val Asp Ser Met Pro Ala Ala Ser Ser Val Lys Lys 5 · 10 Pro Phe Gly Leu Arg Ser Lys Met Gly Lys Trp Cys Cys Arg Cys Phe Pro Cys Cys Arg Glu Ser Gly Lys Ser Asn Val Gly Thr Ser Gly Asp His Asp Asp Ser Ala Met Lys Thr Leu Arg Ser Lys Met Gly Lys Trp 55 Cys Arg His Cys Phe Pro Cys Cys Arg Gly Ser Gly Lys Ser Asn Val Gly Ala Ser Gly Asp His Asp Asp Ser Ala Met Lys Thr Leu Arg Asn Lys Met Gly Lys Trp Cys Cys His Cys Phe Pro Cys Cys Arg Gly Ser 105 Gly Lys Ser Lys Val Gly Ala Trp Gly Asp Tyr Asp Asp Ser Ala Phe 120 Met Glu Pro Arg Tyr His Val Arg Gly Glu Asp Leu Asp Lys Leu His 135 Arg Ala Ala Trp Trp Gly Lys Val Pro Arg Lys Asp Leu Ile Val Met 150 155 Leu Arg Asp Thr Asp Val Asn Lys Lys Asp Lys Gln Lys Arg Thr Ala 170 Leu His Leu Ala Ser Ala Asn Gly Asn Ser Glu Val Val Lys Leu Leu 180 185 Leu Asp Arg Arg Cys Gln Leu Asn Val Leu Asp Asn Lys Lys Arg Thr 200 Ala Leu Ile Lys Ala Val Gln Cys Gln Glu Asp Glu Cys Ala Leu Met 215 220 Leu Leu Glu His Gly Thr Asp Pro Asn Ile Pro Asp Glu Tyr Gly Asn

225					230					235					240
Thi	Thi	. Let	ı His	Ty:		Ile	Тут	Asr	1 Glu 250		Lys	Lev	Met	Ala 259	Lys
Ala	a Lev	ı Let	1 Let 260		Gly	Ala	Asp	11e 265		ı Ser	Lys		Lys 270	His	Gly
Leu	Thi	275		Leu	Leu	Gly	Val 280	His		ı Gln	Lys	Gln 285	Gln	Va]	Val
Lya	290	Leu	Ile	Lys	Lys	Lys 295	Ala		Leu	ı Asn	Ala	Leu		Arg	Tyr
Gly 305	Arg		Ala	Leu	Ile 310	Leu		Val	Cys	Cys 315	Gly		Ala	Ser	Ile
Val	Ser	Leu	Leu	Leu 325	Glu		Asn	Ile				Ser			320 Leu
Ser	Gly	Gln	Thr 340	Ala		Glu	Tyr	Ala	Val	Ser	Ser	His	His		Val
Ile	Cys	Gln 355	Leu		Ser	Asp	Tyr 360	Lys			Gln	Met 365	Leu	Lys	Ile
Ser	Ser 370	Glu		Ser	Asn	Pro 375			Asp	Leu	Lys 380		Thr	Ser	<b>Gl</b> u
Glu 385	Glu		Gln	Arg	Phe 390		Gly	Ser	Glu	Asn 395		Gln	Pro	Glu	Lys 400
Met	Ser	Gln	Glu	Pro 405		Ile	Asn	Lys	Asp 410	Gly	Asp	Arg	Glu	Val 415	Glu
Glu	Glu	Met	Lys 420	Lys	His	Glu	Ser	Asn 425		Val	Gly	Leu	Leu 430	Glu	Asn
Leu	Thr	Asn 435	.Gly	Val	Thr	Ala	Gly 440	Asn	Gly	Asp	Asn	Gly	Leu	Ile	Pro
Gln	Arg 450		Ser	Arg	Thr	Pro 455		Asn	Gln	Gln	Phe 460	Pro	Asp	Asn	Glu
Ser 465	Glu	Glu	Tyr	His	Arg 470	Ile	Сув	Glu	Leu	Val 475			Tyr	Lys	Glu 480
				485					490	Ser			•	495	Asp
Leu	Lys	Leu	Thr 500	Ser	Glu	Glu	Glu	Ser 505	Gln	Arg	Leu	Glu	Gly 510	Ser	Glu
	•	515					520			Pro		525	٠.		
-	530					535			•	Ile	540			Ŧ	_
545	•		•		550			•		Asn 555					560
		•		565					570					575	Arg
			580					585		Glu			590		
Ser	Asp	Glu 595	Gln	Asn	Asp		Gln 600	Lys	Gln	Phe		Glu 605	Glu	Gln	Asn
Thr	Gly 610	Ile	Leu	His		Glu 615	Ile	Leu	Ile	His			Lys	Gln	Ile
Glu 625	Val	Val	Glu	Lys	Met 630	Asn	Ser	Glu		Ser 635		Ser	Cys		Lys 640
				645					Thr 650	Leu				Ile 655	Ala
Met	Leu	Arg	Leu 660	Glu	Leu	Asp		Met 665	Lys	His	Gln		Gln 670	Leu	

60

120

180

24.0

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       <211> 251
       <212> DNA
       <213> Homo sapien
       <400> 381
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 ccaatatccc aggagaagca ttgggggagtt gggggcaggt gaaggaccca ggactcacac
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 caagcagtca g
                                                                       251
<210> 382
<211> 3279
<212> DNA
<213> Homo sapiens
<400> 382
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atgctggagg gtgtcaggaa gtgatcgggc tctggggcag ggaggagggg tggggagtgt 120
cactgggagg ggacatcctg cagaaggtag gagtgagcaa acacccgctg caggggaggg 180
gagagccctg cggcacctgg gggagcagag ggagcagcac ctgcccaggc ctgggaggag 240
gggcctggag ggcgtgagga ggagcgaggg ggctgcatgg ctggagtgag ggatcagggg 300
cagggcgcga gatggcctca cacagggaag agagggcccc tectgcaggg cetcacetgg 360
gccacaggag gacactgctt ttcctctgag gagtcaggag ctgtggatgg tgctggacag 420
aagaaggaca gggcctggct caggtgtcca gaggctgtcg ctggcttccc tttgggatca 480
gactgcaggg agggagggcg gcagggttgt ggggggagtg acgatgagga tgacctgggg 540
gtggctccag gccttgcccc tgcctgggcc ctcacccagc ctccctcaca gtctcctggc 600
cctcagtete teccetecae tecatectee atetggeete agtgggteat tetgateaet 660
gaactgacca tacccagece tgcccacgge estecatgge tececaatge cetggagagg 720
ggacatctag tcagagagta gtcctgaaga ggtggcctct gcgatgtgcc tgtgggggca 780
gcatcctgca gatggtcccg gccctcatcc tgctgacctg tctgcaggga ctgtcctcct 840
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gagccttgtt ccctctgttg gactccctgc ccatattctt gtgggagtgg gttctggaga 960
cattletgte tgtteetgag agetgggaat tgeteteagt catetgeetg egeggttetg 1020
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ttacccttag ggtgattctg ggggtccact tgtctgtaat ggtgtgcttc aaggtatcac 1140
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gcattaccgg aagtggatca aggacaccat cgcagccaac ccctgagtgc ccctgtccca 1260
cccctacctc tagtaaattt aagtccacct cacgttctgg catcacttgg cctttctgga 1320
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tagggggaga aactgaaagc tgattaatta caggaggttt gttcaggtcc cccaaaccac 1860
cgtcagattt gatgatttcc tagcaggact tacagaaata aagagctatc atgctgtggt 1920
ttattatggt ttgttacatt gataggatac atactgaaat cagcaaacaa aacagatgta 1980
tagattagag tgtggagaaa acagaggaaa acttgcagtt acgaagactg gcaacttggc 2040
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gtagctgatc cagctgatag aggaactagc caggtggggg cctttccctt tggatggggg 2160
```

```
gcatatccga cagttattct ctccaagtgg agacttacgg acagcatata attctccctg 2220
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gtgtccaggg tttttactgg gggtctgtag gacgagtatg gagtacttga ataattgacc 2340
tgaagtcctc agacctgagg ttccctagag ttcaaacaga tacagcatgg tccagagtcc 2400
cagatgtaca aaaacaggga ttcatcacaa atcccatctt tagcatgaag ggtctggcat 2460
ggcccaaggc cccaagtata tcaaggcact tgggcagaac atgccaagga atcaaatgtc 2520
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gcagggctgc tgagtcaacc ttttattgta caggggatga gggaaaggga gaggatgagg 2640
aageceeet ggggatttgg tttggtettg tgateaggtg gtetatgggg ctateeetae 2700
aaagaagaat ccagaaatag gggcacattg aggaatgata ctgagcccaa agagcattca 2760
atcattgttt tatttgcctt cttttcacac cattggtgag ggagggatta ccaccctggg 2820
gttatgaaga tggttgaaca ccccacacat agcaccggag atatgagatc aacagtttct 2880
tagccataga gattcacagc ccagagcagg aggacgctgc acaccatgca ggatgacatg 2940
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acaagacggt ggggcaaact ctgatttccg tgggggaatg tcatggtctt gctttactaa 3060
gttttgagac tggcaggtag tgaaactcat taggctgaga accttgtgga atgcagctga 3120
cccagctgat agaggaagta gccaggtggg agcctttccc agtgggtgtg ggacatatct 3180
ggcaagattt tgtggcactc ctggttacag atactggggc agcaaataaa actgaatctt 3240
gttttcagac cttaaaaaaa aaaaaaaaa aaaagtttt
<210> 383
<211> 155
<212> PRT
<213> Homo sapiens
<400> 383
Met Ala Gly Val Arg Asp Gln Gly Gln Gly Ala Arg Trp Pro His Thr
                      10
Gly Lys Arg Gly Pro Leu Leu Gln Gly Leu Thr Trp Ala Thr Gly Gly
                     25
His Cys Phe Ser Ser Glu Glu Ser Gly Ala Val Asp Gly Ala Gly Gln
Lys Lys Asp Arg Ala Trp Leu Arg Cys Pro Glu Ala Val Ala Gly Phe
                  55
Pro Leu Gly Ser Asp Cys Arg Glu Gly Gly Arg Gln Gly Cys Gly Gly
Ser Asp Asp Glu Asp Asp Leu Gly Val Ala Pro Gly Leu Ala Pro Ala
                85
Trp Ala Leu Thr Gln Pro Pro Ser Gln Ser Pro Gly Pro Gln Ser Leu
                               105
Pro Ser Thr Pro Ser Ser Ile Trp Pro Gln Trp Val Ile Leu Ile Thr
                        120
Glu Leu Thr Ile Pro Ser Pro Ala His Gly Pro Pro Trp Leu Pro Asn
   130
Ala Leu Glu Arg Gly His Leu Val Arg Glu
145
                   150
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<211> 557
<212> DNA
<213> Homo sapiens
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ggggaagggt cccttttgca ttgccaagtg ccataaccat gagcactact ctaccatggt 180
tetgeeteet ggeeaageag getggtttge aagaatgaaa tgaatgatte tacagetagg 240
acttaacctt gaaatggaaa gtettgeaat eecatttgea ggateegtet gtgeacatge 300
ctctgtagag agcagcattc ccagggacct tggaaacagt tggcactgta aggtgcttgc 360
tccccaagac acatcctaaa aggtgttgta atggtgaaaa cgtcttcctt ctttattgcc 420
cottottatt tatgtgaaca actgtttgtc tttttttgta tcttttttaa actgtaaagt 480
tcaattgtga aaatgaatat catgcaaata aattatgcga ttttttttc aaagtaaaaa 540
aaaaaaaaa aaaaaaa
                                                                  557
<210> 385
<211> 33.7
<212> DNA
<213> Homo sapiens
<400> 385
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tetcaaagee atetgetgte ttegagtaeg gacacateat cacteetgea ttgttgatea 180
aaacgtggag gtgctttcc tcagctaaga agcccttagc aaaagctcga atagacttag 240
tatcagacag gtocagtttc cgcaccaaca cctgctggtt ccctgtcgtg gtctggatct 300
ctttggccac caattccccc ttttccacat cccggca
<210> 386
<211> 300 -
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<213> Homo sapiens
<400> 386
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gcccgctcgg cccagagggt gggcgcgggg ctgcctctac cggctggcgg ctgtaactca 120
gcgaccttgg cccgaaggct ctagcaagga cccaccgacc ccagccgcgg cggcggcggc 180
geggaetttg eeeggtgtgt ggggeggage ggaetgegtg teegeggaeg ggeagegaag 240
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<210> 387
<211> 537
<212> DNA
<213> Homo sapiens
<400> 387
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tgaaccagga eeggettetg ggeggetgaa aggggcaagg aggcaaggac eeegtetete 180
ccacggatgg ggagagggca ggaggagacc cagccaagtg ccttttcctc agcactgagg 240
gagggggctt gtttcccttc cctcccggcg acaagctcca gggcagggct gtccctctgg 300
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geggeecage acttecteag acaeaactte tteetgetge tecagtegtg gggateatea 360
cttacccacc ccccaagttc aagaccaaat cttccagctg cccccttcgt gtttccctgt 420
gtttgctgta gctgggcatg tctccaggaa ccaagaagcc ctcagcctgg tgtagtctcc 480
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<210> 388
<211> 520
<212> DNA
<213> Homo sapiens
<400> 388
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tgaggttaaa ccagtttgca ttcccctaat gtggaaaaag taagaggact actcagcact 120
gtttgaagat tgcctcttct acagcttctg agaattgtgt tatttcactt gccaagtgaa 180
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ccaggaaact gctacttgtg gacctcacca gagaccagga gggtttggtt agctcacagg 300
acttccccca ccccagaaga ttagcatccc atactagact catactcaac tcaactagge 360
tcatactcaa ttgatggtta ttagacaatt ccatttcttt ctggttatta taaacagaaa 420
atctttcctc ttctcattac cagtaaaggc tcttggtatc tttctgttgg aatgatttct 480
atgaacttgt cttattttaa tggtgggttt tttttctggt
<210> 389
<211> 365
<212> DNA
<213> Homo sapiens
<400> 389
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gagttaaggc tggatttcag atctgcctgg ttccagccgc agtgtgccct ctgctcccc 120
aacgacttte caaataatet caccagegee ttecagetea ggegteetag aagegtettg 180
aageetatgg ceagetgtet ttgtgtteee teteaceege etgteeteae agetgagaet 240
cccaggaaac cttcagacta ccttcctctg ccttcagcaa ggggcgttgc ccacattctc 300
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<210> 390
<211> 221
<212> DNA
<213> Homo sapiens
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<400> 390
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tacacggntt ctcatgggtg tggaacatct ctgcttgcgg tttcaggaag gcctctggct 120
getetangag tetganenga ntegttgeee cantntgaea naaggaaagg eggagettat 180
tcaaagtcta gagggagtgg aggagttaag gctggatttc a
                                                                  221
<210> 391
<211> 325
<212> DNA
<213> Homo sapiens
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<220>
 <221> misc_feature
 <222> (1)...(325)
 <223> n = A,T,C or G
<400> 391
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tagccagggc actgctgcca acagccagtc cnnataccat catgtnaccc ggtgngctct 180
naantingat niccanaged clacecaten tagticiget eleccacegg niaccagece 240
cactgcccag gaatcctaca gccagtaccc tgtcccgacg tctctaccta ccagtacgat 300
gagaceteeg getactacta tgace
<210> 392
<211> 277
<212> DNA
<213> Homo sapiens
<220>
<221> misc_feature
<222> (1)...(277)
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<400> 392
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agteteactt nggenagngn etectaettg agtetettee eeggeetgnn eeagtngnaa 120
antaccanga accgncatgn cttaanaacn nectggtttn tgggttnntc aatgactgca 180
tgcagtgcac caccetgtcc actacgtgat gctgtaggat taaagtctca cagtgggcgg 240
ctgaggatac agcgccgcgt cctgtgttgc tggggaa
<210> 393
<211> 566
<212> DNA
<213> Homo sapiens
<400> 393
actagtccag tgtggtggaa ttcgcggccg cgtcgacgga caggtcagct gtctggctca 60
gtgatctaca ttetgaagtt gtctgaaaat gtcttcatga ttaaattcag cctaaacgtt 120
ttgccgggaa cactgcagag acaatgctgt gagtttccaa ccttagccca tctgcgggca 180
gagaaggtct agtttgtcca tcagcattat catgatatca ggactggtta cttggttaag 240
gaggggtcta ggagatctgt cccttttaga gacaccttac ttataatgaa gtatttggga 300
gggtggtttt caaaagtaga aatgtcctgt attccgatga tcatcctgta aacatttat 360
catttattaa tcatccctgc ctgtgtctat tattatattc atatctctac gctggaaact 420
cattetetge etgagtttta atttttgtee aaagttattt taatetatae aattaaaage 540
ttttgcctat caaaaaaaa aaaaaa
                                                                566
<210> 394
<211> 384
<212> DNA
<213> Homo sapiens
<220>
<221> misc_feature
```

```
<222> (1)...(384)
 <223> n = A,T,C or G
 <400> 394
 gaacatacat gtcccggcac ctgagctgca gtctgacatc atcgccatca cgggcctcgc 60
 tgcaaattng gaccgggcca aggctggact gctggagcgt gtgaaggagc tacaggccna 120
gcaggaggac cgggctttaa ggagttttaa gctgagtgtc actgtagacc ccaaatacca 180
 teccaagatt ategggagaa agggggeagt aattacccaa ateeggttgg ageatgaegt 240
 gaacatccag tttcctgata aggacgatgg gaaccagccc caggaccaaa ttaccatcac 300
 agggtacgaa aagaacacag aagctgccag ggatgctata ctgagaattg tgggtgaact 360
 tgagcagatg gtttctgagg acgt
 <210> 395
 <211> 399
 <212> DNA
 <213> Homo sapiens
<400> 395
ggcaaaactg tgtgacctca ataagacctc gcagatccaa ggtcaagtat cagaagtgac 60
tetgacettg gaetecaaga eetacateaa eageetgget atattagatg atgageeagt 120
tatcagaggt ttcatcattg cggaaattgt ggagtctaag gaaatcatgg cctctgaagt 180
attcacgtct ttccagtacc ctgagttctc tatagagttg cctaacacag gcagaattgg 240
ccagctactt gtctgcaatt gtatcttcaa gaataccctg gccatccctt tgactgacgt 300
caagttetet tiggaaagee igggeatete eteactacag aceteigace aigggaeggt 360%
gcagcctggt gagaccatcc aatcccaaat aaaatgcac
<210> 396
<211> 403
<212> DNA
<213> Homo sapiens
<220>
<221> misc_feature
<222> (1)...(403)
<223> n = A,T,C or G
<400> 396
tggagttntc agtgcaaaca agccataaag.cttcagtagc aaattactgt ctcacagaaa 60
gacattttca acttctgctc cagctgctga taaaacaaat catgtgttta gcttgactcc 120
agacaaggac aacctgttcc ttcataactc tctagagaaa aaaaggagtt gttagtagat 180
actaaaaaaa gtggatgaat aatctggata tttttcctaa aaagattcct tgaaacacat 240
taggaaaatg gagggcctta tgatcagaat gctagaatta gtccattgtg ctgaagcagg 300
gtttagggga gggagtgagg gataaaagaa ggaaaaaaag aagagtgaga aaacctattt 360
atcaaagcag gtgctatcac tcaatgttag gccctgctct ttt
<210> 397
<211> 100
<212> DNA
<213> Homo sapiens
<220>
<221> misc feature
<222> (1)...(100)
<223> n = A,T,C or G
```

```
<400> 397
actagincag tgiggiggaa ticgcggccg cgicgaccta naanccatci ciatagcaaa 60
tccatccccg ctcctggttg gtnacagaat gactgacaaa
                                                                 100
 <210> 398
 <211> 278
<212> DNA
<213> Homo sapiens
<220>
<221> misc feature
<222> (1)...(278)
\langle 223 \rangle n = A,T,C or G
<400> 398
geggeegegt egacageagt teegeeageg etegeeeetg ggtggggatg tgetgeacge 60
ccacctggac atctggaagt cagcggcctg gatgaaagag cggacttcac ctggggcgat 120
tcactactgt gcctcgacca gtgaggagag ctggaccgac agcgaggtgg actcatcatg 180
ctccgggcag cccatccacc tgtggcagtt cctcaaggag ttgctactca agccccacag 240
ctatggccgc ttcattangt ggctcaacaa ggagaagg
<210> 399
<211> 298
<212> DNA
<213> Homo sapiens
<220>
<221> misc_feature
<222> (1)...(298)
<223> n = A,T,C or G
<400> 399
acggaggtgg aggaagcgnc cctgggatcg anaggatggg tcctgncatt gaccncctcn 60
ggggtgccng catggagcgc atgggcgcgg gcctgggcca cggcatggat cgcgtgggct 120
ccgagatcga gcgcatgggc ctggtcatgg accgcatggg ctccgtggag cgcatgggct 180
ccggcattga gcgcatgggc ccgctgggcc tcgaccacat ggcctccanc attgancgca 240
tgggccagac catggagcgc attggctctg gcgtggagcn catgggtgcc ggcatggg
<210> 400
<211> 548
<212> DNA
<213> Homo sapiens
<400> 400
acatcaacta cttcctcatt ttaaggtatg gcagttccct tcatcccctt ttcctgcctt 60
gtacatgtac atgtatgaaa tttccttctc ttaccgaact ctctccacac atcacaaggt 120
tgagtctctt ttttccacgt ttaaggggcc atggcaggac ttagagttgc gagttaagac 240
tgcagagggc tagagaatta tttcatacag gctttgaggc cacccatgtc acttatcccg 300
tataccetet caccatecce ttgtetacte tgatgecece aagatgeaac tgggcageta 360
gttggcccca taattctggg cctttgttgt ttgttttaat tacttgggca tcccaggaag 420
ctttccagtg atctcctacc atgggccccc ctcctgggat caagcccctc ccaggccctg 480
tecceagese etectgoese agescaeseg ettgeettgg tgeteagese teccattggg 540
agcaggtt
```

```
<210> 401
<211> 355
<212> DNA
<213> Homo sapiens
<220>
<221> misc_feature
<222> (1) ... (355)
<223> n = A,T,C or G
<400> 401
actgtttcca tgttatgttt ctacacattg ctacctcagt gctcctggaa acttagcttt 60
tgatgtctcc aagtagtcca ccttcattta actctttgaa actgtatcat ctttgccaag 120
taagagtggt ggcctatttc agctgctttg acaaaatgac tggctcctga cttaacgttc 180
tataaatgaa tgtgctgaag caaagtgccc atggtggcgg cgaagaagan aaagatgtgt 240
tttgttttgg actctctgtg gtcccttcca atgctgnggg tttccaacca ggggaagggt 300
cccttttgca ttgccaagtg ccataaccat gagcactact ctaccatggn tctgc
<210> 402
<211> 407
<212> DNA
<213> Homo sapiens
<220>
<221> misc_feature
<222> (1) ... (407)
<223> n = A,T,C or G
<400> 402
atggggcaag ctggataaag aaccaagacc cactggagta tgctgtcttc aagaaaccca 60
tctcacatgc ggtggcatac ataggctcaa aataaaggaa tggagaaaaa tatttcaagc 120
aaatggaaaa cagaaaaaag caggtgttgc actcctactt tctgacaaaa cagactatgc 180
gaataaagat aaaaaagaga aggacattac aaaggtggtc ctgacctttg ataaatctca 240
ttgcttgata ccaacctggg ctgttttaat tgcccaaacc aaaaggataa tttgctgagg 300
ttgtggagct tctcccctgc agagagtccc tgatctccca aaatttggtt gagatgtaag 360
gntgattttg ctgacaactc cttttctgaa gttttactca tttccaa
                                                                   407
<210> 403
<211> 303
<212> DNA
<213> Homo sapiens
<220>
<221> misc_feature
<222> (1)...(303)
<223> n = A,T,C or G
<400> 403
cagtatttat agccnaactg aaaagctagt agcaggcaag tctcaaatcc aggcaccaaa 60
tcctaagcaa gagccatggc atggtgaaaa tgcaaaagga gagtctggcc aatctacaaa 120
tagagaacaa gacctactca gtcatgaaca aaaaggcaga caccaacatg gatctcatgg 180
gggattggat attgtaatta tagagcagga agatgacagt gatcgtcatt tggcacaaca 240
tottaacaac gaccgaaacc cattatttac ataaacctcc attcggtaac catgttgaaa 300
gga
                                                                  303
```

```
<210> 404
<211> 225
<212> DNA
<213> Homo sapiens
<400> 404
aagtgtaact tttaaaaatt tagtggattt tgaaaattct tagaggaaag taaaggaaaa 60
attgttaatg cactcattta cctttacatg gtgaaagttc tctcttgatc ctacaaacag 120
acattttcca ctcgtgtttc catagttgtt aagtgtatca gatgtgttgg gcatgtgaat 180
ctccaagtgc ctgtgtaata aataaagtat ctttatttca ttcat
<210> 405
<211> 334
<212> DNA
<213> Homo sapiens
<220>
<221> misc feature
<222> (1) ... (334)
<223> n = A,T,C or G
<400> 405
gagetgttat aetgtgagtt etaetaggaa ateateaaat etgagggttg tetggaggae 60
ttcaatacac ctcccccat agtgaatcag cttccagggg gtccagtccc tctccttact 120
teatececat eccatgeeaa aggaagacee teecteettg geteacagee ttetetagge 180
ttcccagtgc ctccaggaca gagtgggtta tgttttcagc tccatccttg ctgtgagtgt 240
ctggtgcggt tgtgcctcca gcttctgctc agtgcttcat ggacagtgtc cagcccatgt 300
cactetecae teteteanng tggateceae eeet
<210> 406
<211> 216
<212> DNA
<213> Homo sapiens
<220> .:.
<221> misc_feature
<222<sub>>(1)...(216)</sub>
\langle 223 \rangle n = A,T,C or G
<400> 406
tttcatacct aatgagggag ttganatnac atnnaaccag gaaatgcatg gatctcaang 60
gaaacaaaca cecaataaac teggagtgge agactgacaa etgtgagaca tgcacttget 120
acnaaacaca aatttnatgt tgcacccttg tttctacacc tgtgggttat gacaaagaca 180
actgccaaag aatnttcaag aaggaggact gccant
                                                                    216
<210> 407
<211> 413
<212> DNA
<213> Homo sapiens
<400> 407
gctgacttgc tagtatcatc tgcattcatt gaagcacaag aacttcatgc cttgactcat 60
gtaaatgcaa taggattaaa aaataaattt gatatcacat ggaaacagac aaaaaatatt 120
gtacaacatt gcacccagtg tcagattcta cacctggcca ctcaggaagc aagagttaat 180
cccagaggtc tatgtcctaa tgtgttatgg caaatggatg tcatgcacgt accttcattt 240
```

```
ggaaaattgt catttgtcca tgtgacagtt gatacttatt cacatttcat atgggcaacc 300
 tgccagacag gagaaagtct tcccatgtta aaagacattt attatcttgt tttcctgtca 360
 tgggagttcc agaaaaagtt aaaacagaca atgggccagg ttctgtagta aag
 <210> 408
 <211> 183
 <212> DNA
 <213> Homo sapiens
 <220>
 <221> misc_feature
 <222> (1)...(183)
 <223> n = A,T,C or G
 <400> 408
ggagetngee etcaatteet ecatniciat gitaneatat tiaatgiett tignnatiaa 60
tncttaacta gttaatcctt aaagggctan ntaatcctta actagtccct ccattgtgag 120
cattateett ecagtatten cettetnttt tatttactee tteetggeta eccatgtact 180
ntt
<210> 409
<211> 250
<212> DNA
<213> Homo sapiens
<220>
<221> misc feature .
<222> (1)...(250)
<223> n = A,T,C or G
<400> 409.
cccacgcatg ataagctett tatttetgta agteetgeta ggaaatcate aaatetgaeg 60
gtggtttggg ggacctgaac aaacctcctg taattaatca gctttcagtt tctcccccta 120
gtccctcctt caacaacata ggaggatcct ccccttcttt ctgctcacgg ccttatctag 180
getteecagt geeecagga cagegtggge tatgtttaca gegenteett getggggggg 240
ggccntatgc
<210> 410
<211> 306
<212> DNA
<213> Homo sapiens
<220>
<221> misc_feature
<222> (1)...(306)
<223> n = A,T,C \text{ or } G
<400> 410
ggctggtttg caagaatgaa atgaatgatt ctacagctag gacttaacct tgaaatggaa 60
agtettgeaa teecatttge aggateegte tgtgeacatg eetetgtaga gageageatt 120
cccagggacc ttggaaacag ttggcactgt aaggtgcttg ctccccaaga cacatcctaa 180
aaggtgttgt aatggtgaaa accgcttcct tctttattgc cccttcttat ttatgtgaac 240
nactggttgg ctttttttgn atcttttta aactggaaag ttcaattgng aaaatgaata 300
tcntgc
```

```
<210> 411
 <211> 261
 <212> DNA
 <213> Homo sapiens
 <220>
 <221> misc_feature
 <222> (1) ... (261)
 \langle 223 \rangle n = A,T,C or G
 <400> 411
 agagatattn cttaggtnaa agttcataga gttcccatga actatatgac tggccacaca 60
 ggatcttttg tatttaagga ttctgagatt ttgcttgagc aggattagat aaggctgttc 120
 tttaaatgtc tgaaatggaa cagatttcaa aaaaaaaccc cacaatctag ggtgggaaca 180
 aggaaggaaa gatgtgaata ggctgatggg caaaaaacca atttacccat cagttccagc 240
 cttctctcaa ggngaggcaa a
                                                                     261
 <210> 412
 <211> 241 .
 <212> DNA
 <213> Homo sapiens
 <220>
 <221> misc feature
 <222> (1)...(241)
 <223> n = A,T,C or G
<400> 412
 gttcaatgtt acctgacatt tctacaacac cccactcacc gatgtattcg ttgcccagtg 60
 ggaacatacc agcctgaatt tggaaaaaat aattgtgttt cttgcccagg aaatactacg 120
 actgactttg atggctccac aaacataacc cagtgtaaaa acagaagatg tggagggag 180
 ctgggagatt tcactgggta cattgaattc ccaaactacc cangcaatta cccagccaac 240
 <210> 413
 <211> 231
 <212> DNA
 <213> Homo sapiens
 <220>
 <221> misc_feature
 <222> (1)...(231)
 <223> n = A,T,C \text{ or } G
 <400> 413
 aactettaca atccaagtga ctcatctgtg tgcttgaate ctttccactg tctcatctcc 60
 ctcatccaag tttctagtac cttctctttg ttgtgaagga taatcaaact gaacaacaaa 120
 aagtttactc tcctcatttg gaacctaaaa actctcttct tcctgggtct gagggctcca 180
 agaatccttg aatcanttct cagatcattg gggacaccan atcaggaacc t
 <210> 414
 <211> 234
 <212> DNA
 <213> Homo sapiens
```

<400> 414

```
actgtccatg aagcactgag cagaagctgg aggcacaacg caccagacac tcacagcaag 60
 gatggagctg aaaacataac ccactctgtc ctggaggcac tgggaagcct agagaaggct 120
 gtgagccaag gagggagggt cttcctttgg catgggatgg ggatgaagta aggagaggga 180
 ctggaccccc tggaagctga ttcactatgg ggggaggtgt attgaagtcc tcca
 <210> 415
 <211> 217
 <212> DNA
 <213> Homo sapiens
 <220>
 <221> misc_feature
 <222> (1)...(217)
 <223> n = A,T,C or G
 <400> 415
gcataggatt aagactgagt atcttttcta cattctttta actttctaag gggcacttct 60
caaaacacag accaggtagc aaatctccac tgctctaagg ntctcaccac cactttctca 120
cacctagcaa tagtagaatt cagtcctact tctgaggcca gaagaatggt tcagaaaaat 180
antggattat aaaaaataac aattaagaaa aataatc
<210> 416
<211> 213
<212> DNA
<213> Homo sapiens
<220>
<221> misc_feature
<222> (1)...(213)
<223> n = A,T,C or G
<400> 416
atgcatatnt aaagganact gcctcgcttt tagaagacat ctggnctgct ctctgcatga 60
ggcacagcag taaagctctt tgattcccag aatcaagaac tctccccttc agactattac 120
cgaatgcaag gtggttaatt gaaggccact aattgatgct caaatagaag gatattgact 180
atattggaac agatggagtc tctactacaa aag
<210> 417
<211> 303
<212> DNA
<213> Homo sapiens
<220>
<221> misc feature
<222> (1)...(303)
<223> n = A,T,C or G
<400> 417
nagtetteag geceateagg gaagtteaca etggagagaa gteatacata tgtaetgtat 60
gtgggaaagg ctttactctg agttcaaatc ttcaagccca tcagagagtc cacactggag 120
agaagccata caaatgcaat gagtgtggga agagcttcag gagggattcc cattatcaag 180
ttcatctagt ggtccacaca ggagagaaac cctataaatg tgagatatgt gggaagggct 240
tcantcaaag ttcgtatctt caaatccatc ngaaggncca cagtatanan aaacctttta 300
agt
```

<211> 352 <212> DNA

```
<210> 418
<211> 328
<212> DNA
<213> Homo sapiens
<220>
<221> misc_feature
<222> (1)...(328)
<223> n = A,T,C or G
<400> 418
tttttggegg tggtggggca gggaegggae angagtetea etetgttgee caggetggag 60
tgcacaggca tgatctcggc tcactacaac ccctgcctcc catgtccaag cgattcttgt 120
gcctcagcct tccctgtagc tagaattaca ggcacatgcc accacaccca gctagttttt 180
gtatttttag tagagacagg gtttcaccat gttggccagg ctggtctcaa actcctnacc 240
teagnggtea ggetggtete aaacteetga eetcaagtga tetgeecace teageeteec 300
aaagtgctan gattacaggc cgtgagcc
                                                                   328
<210> 419
<211> 389.
<212> DNA
<213> Homo sapiens
<220>
<221> misc_feature
<222> (1)...(389)
<223> n = A,T,C or G
<400> 419
cctcctcaag acggcctgtg gtccgcctcc cggcaaccaa gaagcctgca gtgccatatg 60
acccetgage catggactgg agcctgaaag gcagcgtaca ccctgctcct gatettgctg 120
cttgtttcct ctctgtggct ccattcatag cacagttgtt gcactgaggc ftgtgcaggc 180
cgagcaaggc caagctggct Caaagagcaa ccagtcaact ctgccacggt gtgccaggca 240
ceggttetec agecaceaac etcacteget ecegeaaatg geacateagt tettetacec 300
taaaggtagg accaaagggc atctgctttt ctgaagtcct ctgctctatc agccatcacg 360
tggcagccac tenggetgtg tegacgegg
<210> 420
<211> 408
<212> DNA
<213> Homo sapiens
<400> 420
gttectecta actectgeca gaaacagete tecteaacat gagagetgea ecectectee 60
tggccagggc agcaagcctt agccttggct tcttgtttct gcttttttc tggctagacc 120
gaagtgtact agccaaggag ttgaagtttg tgactttggt gtttcggcat ggagaccgaa 180
gtcccattga cacctttccc actgacccca taaaggaatc ctcatggcca caaggatttg 240
gccaactcac ccagctgggc atggagcagc attatgaact tggagagtat ataaqaaaqa 300
gatatagaaa attottgaat gagtootata aacatgaaca ggtttatatt cgaagcacag 360
acgttgaccg gactttgatg aagtgctatg acaaacctgg caagcccg
                                                                   408
<210> 421
```

<213> Homo sapiens

```
<220>
 <221> misc_feature
 <222> (1)...(352)
 <223> n = A,T,C or G
 <400> 421
 gctcaaaaat ctttttactg atnggcatgg ctacacaatc attgactatt acggaggcca 60
gaggagaatg aggcctggcc tgggagccct gtgcctacta naagcacatt agattatcca 120
ttcactgaca gaacaggtct tttttgggtc cttcttctcc accacnatat acttgcagtc 180
ctccttcttg aagattcttt ggcagttgtc tttgtcataa cccacaggtg tagaaacaag 240
ggtgcaacat gaaatttctg tttcgtagca agtgcatgtc tcacaagttg gcangtctgc 300
cacteegagt ttattgggtg tttgttteet ttgagateea tgeattteet gg
<210> 422
 <211> 337
<212> DNA
<213> Homo sapiens
<400> 422
atgccaccat gctggcaatg cagcgggcgg tcgaaggcct gcatatccag cccaagctgg 60
cgatgatcga cggcaaccgt tgcccgaagt tgccgatgcc agccgaagcg gtggtcaagg 120
gcgatagcaa ggtgccggcg atcgcggcgg cgtcaatcct ggccaaggtc agccgtgatc 180
gtgaaatggc agctgtcgaa ttgatctacc cgggttatgg catcggcggg cataagggct 240
atccgacacc ggtgcacctg gaagcettgc agcggctggg gccgacgccg attcaccgac 300
gcttcttccg ccggtacggc tggcctatga aaattat
<210> 423
<211> 310
<212> DNA
<213> Homo sapiens
<220>
<221> misc feature
<222> (1) ... (310)
<223> n = A,T,C or G
<400> 423
gctcaaaaat ctttttactg atatggcatg gctacacaat cattgactat tagaggccag 60
aggagaatga ggcctggcct gggagccctg tgcctactan aagcncatta gattatccat 120
tcactgacag aacaggtctt ttttgggtcc ttcttctcca ccacgatata cttgcagtcc 180
tccttcttga agattctttg gcagttgtct ttgtcataac ccacaggtgt anaaacaagg 240
gtgcaacatg aaatttctgt ttcgtagcaa gtgcatgtct cacagttgtc aagtctgccc 300
tccgagttta
<210> 424
<211> 370
<212> DNA -
<213> Homo sapiens
<220>
<221> misc feature
<222> (1)...(370)
\langle 223 \rangle n = A,T,C or G
```

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```
<400> 424
gctcaaaaat ctttttactg ataggcatgg ctacacaatc attgactatt agaggccaga 60
ggagaatgag gcctggcctg ggagccctgt gcctactaga agcacattag attatccatt 120
cactgacaga acaggtettt tttgggteet tetteteeac cacgatatac ttgcagteet 180
ccttcttgaa gattctttgg cagttgtctt tgtcataacc cacaggtgta gaaacatcct 240
ggttgaatct cctggaactc cctcattagg tatgaaatag catgatgcat tgcataaagt 300
cacgaaggtg gcaaagatca caacgctgcc cagganaaca ttcattgtga taagcaggac 360
<210> 425
<211> 216
<212> DNA
<213> Homo sapiens
<220>
<221> misc feature
<222> (1)...(216)
<223> n = A,T,C or G
<400> 425
taacaacnca acatcaaggn aaananaaca ggaatggntg actntgcata aatnggccga 120
anattateca ttatnttaag ggttgactte aggntacage acacagacaa acatgeecag 180
gaggntntca ggaccgctcg atgtnttntg aggagg
                                                                216
<210> 426
<211> 596
<212> DNA
<213> Homo sapiens
<400> 426
cttccagtga ggataaccct gttgccccgg gccgaggttc tccattaggc tctgattgat 60 ...
tggcagtcag tgatggaagg gtgttctgat cattccgact gccccaaggg tcgctggcca 120
gctctctgtt ttgctgagtt ggcagtagga cctaatttgt taattaagag tagatggtga 180 👈
gctgtccttg tattttgatt aacctaatgg ccttcccagc acgactcgga ttcagctgga 240
gacatcacgg caacttttaa tgaaatgatt tgaagggcca ttaagaggca cttcccqtta 300
ttaggcagtt catctgcact gataacttct tggcagctga gctggtegga gctgtggccc 360
aaacgcacac ttggcttttg gttttgagat acaactctta atcttttagt catgcttgag 420
ggtggatggc cttttcagct ttaacccaat ttgcactgcc ttggaagtgt agccaggaga 480
atacactcat atactcgtgg gcttagaggc cacagcagat gtcattggtc tactgcctga 540
gtcccgctgg tcccatccca ggaccttcca tcggcgagta cctgggagcc cgtgct
<210> 427
<211> 107
<212> DNA
<213> Homo sapiens
<220>
<221> misc_feature
<222> (1)...(107)
<223> n = A,T,C or G
<400> 427
gaagaattca agttaggttt attcaaaggg cttacngaga atcctanacc caggncccag 60
```

```
cccgggagca gccttanaga gctcctgttt gactgcccgg ctcagng
                                                                    107
 <210> 428
 <211> 38
 <212> DNA
 <213> Homo sapiens
 <220>
 <221> misc_feature
 <222> (1) ... (38)
<223> n = A,T,C or G
<400> 428
gaacttccna anaangactt tattcactat tttacatt
                                                                    38
<210> 429
<211> 544
<212> DNA
<213> Homo sapiens
<400> 429
ctttgctgga cggaataaaa gtggacgcaa gcatgacctc ctgatgaggg cgctgcattt 60
attgaagagc ggctgcagcc ctgcggttca gattaaaatc cgagaattgt atagacgccg 120
atatccacga actettgaag gaetttetga tttatccaca atcaaatcat eggtttteag 180
tttggatggt ggctcatcac ctgtagaacc tgacttggcc gtggctggaa tccactcgtt 240
gccttccact tcagttacac ctcactcacc atcctctcct gttggttctg tgctgcttca 300
agatactaag cccacatttg agatgcagca gccatctccc ccaattcctc ctgtccatec 360
tgatgtgcag ttaaaaaatc tgccctttta tgatgtcctt gatgttctca tcaagcccac 420
gagtttagtt caaagcagta ttcagcgatt tcaagagaag ttttttattt ttgctttgac 480
acctcaacaa gttagagaga tatgcatatc cagggatttt ttgccaggtg gtaggagaga 540
ttat
<210> 430
<211> 507
<212> DNA
<213> Homo sapiens
<220>
<221> misc_feature
<222> (1)...(507)
<223> n = A,T,C or G
<400> 430
cttatcncaa tggggctccc aaacttggct gtgcagtgga aactccgggg gaattttgaa 60
gaacactgac acccatcttc caccccgaca ctctgattta attgggctgc agtgagaaca 120
gagcatcaat ttaaaaagct gcccagaatg ttntcctggg cagcgttgtg atctttgccn 180
ccttcgtgac tttatgcaat gcatcatgct atttcatacc taatgaggga gttccaggag 240
attcaaccag gatgtttcta cncctgtggg ttatgacaaa gacaactgcc aaagaatntt 300
caagaaggag gactgcaagt atatcgtggt ggagaagaag gacccaaaaa agacctgttc 360
tgtcagtgaa tggataatct aatgtgcttc tagtaggcac agggctccca ggccaggcct 420
catteteete tggeetetaa tagteaatga ttgtgtagee atgeetatea gtaaaaagat 480
ttttgagcaa aaaaaaaaa aaaaaaa
                                                                  507
<210> 431
<211> 392
```

```
<212> DNA
 <213> Homo sapiens
<220>
<221> misc_feature
<222> (1)...(392)
<223> n = A,T,C or G
<400> 431
gaaaattcag aatggataaa aacaaatgaa gtacaaaata tttcagattt acatagcgat 60
aaacaagaaa gcacttatca ggaggactta caaatggaag tacactctan aaccatcatc 120
tatcatggct aaatgtgaga ttagcacagc tgtattattt gtacattgca aacacctaga 180
aagagatggg aaacaaaatc ccaggagttt tgtgtgtgga gtcctgggtt ttccaacaga 240
catcattcca gcattctgag attagggnga ttggggatca ttctggagtt ggaatqttca 300
acaaaagtga tgttgttagg taaaatgtac aacttctgga tctatgcaga cattgaaggt 360
gcaatgagtc tggcttttac tctgctgttt ct
<210> 432
<211> 387
<212> DNA
<213> Homo sapiens
<220>
<221> misc_feature
<222> (1) . . . (387)
<223> n = A, T, C or G
<400> 432
ggtatecnta cataatcaaa tatagetgta gtacatgttt teattggngt agattaceae 60
aaatgcaagg caacatgtgt agatetettg tettattett ttgtetataa tactgtattg 120
ngtagtccaa geteteggna gtecagecae tgngaaacat getecettta gattaacete 180
gtggacnetn ttgttgnatt gtetgaactg tagngeeetg tattttgett etgtetgnga 240
attetgttge ttetggggea ttteettgng atgeagagga ceaecaeae gatgaeagea 300
atctgaattg ntccaatcac agctgcgatt aagacatact gaaatcgtac aggaccggga 360
acaacgtata gaacactgga gtccttt
                                                                   387
·<210> 433
<211> 281
<212> DNA
<213> Homo sapiens
<220>
<221> misc feature
<222> (1) . . . (281)
<223> n = A, T, C or G
<400> 433
ttcaactagc anagaanact gcttcagggn gtgtaaaatg aaaggcttcc acgcagttat 60
ctgattaaag aacactaaga gagggacaag gctagaagcc gcaggatgtc tacactatag 120
caggenetat ttgggttgge tggaggget gtggaaaaca tggagagatt ggegetggag 180
ategeogtgg ctattecten ttgntattae accagngagg ntetetgtnt geccaetggt 240
tnnaaaaccg ntatacaata atgatagaat aggacacaca t
<210> 434
<211> 484
```

```
<212> DNA
 <213> Homo sapiens
 <400> 434
ttttaaaata agcatttagt geteagteee tactgagtac tetttetete ceeteetetg 60
aatttaattc tttcaacttg caatttgcaa ggattacaca tttcactgtg atgtatattg 120
tgttgcaaaa aaaaaaaagt gtctttgttt aaaattactt ggtttgtgaa tccatcttgc 180
tttttcccca ttggaactag tcattaaccc atctctgaac tggtagaaaa acatctgaag 240
agctagtcta tcagcatctg acaggtgaat tggatggttc tcagaaccat ttcacccaga 300
cagcctgttt ctatcctgtt taataaatta gtttgggttc tctacatgca taacaaaccc 360
tgctccaatc tgtcacataa aagtctgtga cttgaagttt agtcagcacc cccaccaaac 420
tttatttttc tatgtgtttt ttgcaacata tgagtgtttt gaaaataaag tacccatgtc 480
ttta
                                                                   484
<210> 435
<211> 424
<212> DNA
<213> Homo sapiens
<400> 435
gcgccgctca gagcaggtca ctttctgcct tccacgtcct ccttcaagga agccccatgt 60
gggtagcttt caatatcgca ggttcttact cctctgcctc tataagctca aacccaccaa 120
cgatcgggca agtaaacccc ctccctcgcc gacttcggaa ctggcgagag ttcagcgcag 180
atgggcctgt ggggaggggg caagatagat gagggggagc ggcatggtgc ggggtgaccc 240
cttggagaga ggaaaaaggc cacaagaggg gctgccaccg ccactaacgg agatggccct 300
ggtagagacc tttgggggtc tggaacctct ggactcccca tgctctaact cccacactct 360
gctatcagaa acttaaactt gaggattttc tctgtttttc actcgcaata aattcagagc 420
aaac
<210> 436
<211> 667
<212> DNA
<213> Homo sapiens
<220>
<221> misc_feature
<222> (1)...(667)
<223> n = A,T,C \text{ or } G
<400> 436
accttgggaa nactctcaca atataaaggg tcgtagactt tactccaaat tccaaaaagg 60
tcctggccat gtaatcctga aagttttccc aaggtagcta taaaatcctt ataagggtgc 120
agestettet ggaatteste tgattteaaa gtetsastet caagttettg aaaacgaggg 180
cagtteetga aaggeaggta tageaactga tetteagaaa gaggaactgt gtgeaceggg 240
atgggctgcc agagtaggat aggattccag atgctgacac cttctggggg aaacagggct 300
gccaggtttg tcatagcact catcaaagtc cggtcaacgt ctgtgcttcg aatataaacc 360
tgttcatgtt tataggactc attcaagaat tttctatatc tctttcttat atactetcca 420
agttcataat gctgctccat gcccagctgg gtgagttggc caaatccttg tggccatgag 480
gattccttta tggggtcagt gggaaaggtg tcaatgggac ttcggtctcc atgccgaaac 540
accaaagtca caaacttcaa ctccttggct agtacacttc ggtctagcca gaaaaaaagc 600
agaaacaaga agccaaggct aaggcttgct gccctgccag gaggaggggt gcagctctca 660
tgttgag
                                                                  667
```

<210> 437

<211> 693

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<212> DNA
 <213> Homo sapiens
 <400> 437
ctacgtctca accetcattt ttaggtaagg aatettaagt ccaaagatat taagtgactc 60
acacagccag gtaaggaaag ctggattggc acactaggac tctaccatac cgggttttgt 120
taaagctcag gttaggaggc tgataagctt ggaaggaact tcagacagct ttttcagatc 180
ataaaagata attettagee catgttette teeagageag acetgaaatg acageacage 240
aggtactcct ctattttcac ccctcttgct tctactctct ggcagtcaga cctgtgggag 300
gccatgggag aaagcagctc tctggatgtt tgtacagatc atggactatt ctctgtggac 360
cattleteca ggttacceta ggtgteacta ttggggggac agecageate tttagettte 420
atttgagttt ctgtctgtct tcagtagagg aaacttttgc tcttcacact tcacatctga 480
acacctaact gctgttgctc ctgaggtggt gaaagacaga tatagagctt acagtattta 540
tectatttet aggeactgag ggetgtgggg tacettgtgg tgecaaaaca gateetgttt 600
taaggacatg ttgcttcaga gatgtctgta actatctggg ggctctgttg gctctttacc 660
ctgcatcatg tgctctcttg gctgaaaatg acc
<210> 438
<211> 360
<212> DNA
<213> Homo sapiens
<400> 438
ctgcttatca caatgaatgt tctcctgggc agcgttgtga tctttgccac cttcgtgact 60
ttatgcaatg catcatgcta tttcatacct aatgagggag ttccaggaga ttcaaccagg 120
atgtttctac acctgtgggt tatgacaaag acaactgcca aagaatcttc aagaaggagg 180
actgcaagta tatctggtgg agaagaagga cccaaaaaag acctgttctg tcagtgaatg 240
gataatctaa tgtgcttcta gtaggcacag ggctcccagg ccaggcctca ttctcctctg 300
geetetaata gteaataatt gtgtageeat geetateagt aaaaagattt ttgageaaac 360
<210> 439
<211> 431
<212> DNA
<213> Homo sapiens
<220>
<221> misc_feature
<222> (1) ... (431)
<223> n = A,T,C or G
<400> 439 -
gttectnnta actectgeca gaaacagete tecteaacat gagagetgea eccetectee 60
tggccagggc agcaagcctt agccttggct tcttgtttct gcttttttc tggctagacc 120
gaagtgtact agccaaggag ttgaagtttg tgactttggt gtttcggcat ggagaccgaa 180
gtcccattga cacctttccc actgacccca taaaggaatc ctcatggcca caaggatttg 240
gccaactcac ccagctgggc atggagcagc attatgaact tggagagtat ataagaaaga 300
gatatagaaa attettgaat gagteetata aacatgaaca ggtttatatt egaaqeacaq 360
acgttgaccg gactttgatg agtgctatga caaacctggc agcccgtcga cgcggccgcg 420
aatttagtag t
                                                                  431
<210> 440
<211> 523
<212> DNA
<213> Homo sapiens
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<400> 440
agagataaag cttaggtcaa agttcataga gttcccatga actatatgac tggccacaca 60
ggatcttttg tatttaagga ttctgagatt ttgcttgagc aggattagat aaggctgttc 120
tttaaatgtc tgaaatggaa cagatttcaa aaaaaaaccc cacaatctag ggtgggaaca 180
aggaaggaaa gatgtgaata ggctgatggg caaaaaaacca atttacccat cagttccagc 240
cttctctcaa ggagaggcaa agaaaggaga tacagtggag acatctggaa agttttctcc 300
actggaaaac tgctactatc tgtttttata tttctgttaa aatatatgag gctacagaac 360
taaaaattaa aacctctttg tgtcccttgg tcctggaaca tttatgttcc ttttaaagaa 420
acaaaaatca aactttacag aaagatttga tgtatgtaat acatatagca gctcttgaag 480
tatatatatc atagcaaata agtcatctga tgagaacaag cta
<210> 441
<211> 430
<212> DNA
<213> Homo sapiens
<400> 441
gttcctccta actcctgcca gaaacagctc tcctcaacat gagagctgca cccctcctcc 60
tggccagggc agcaagcctt agccttggct tcttgtttct gcttttttc tggctagacc 120
gaagtgtact agccaaggag ttgaagtttg tgactttggt gtttcggcat ggagaccgaa 180
gtcccattga cacctttccc actgacccca taaaggaatc ctcatggcca caaggatttg 240
gccaactcac ccagctgggc atggagcagc attatgaact tggagagtat ataagaaaga 300
gatatagaaa attettgaat gagteetata aacatgaaca ggtttatatt cgaagcacag 360
acgttgaccg gactttgatg agtgctatga caaacctggc agcccgtcga cgcggccgcg 420
aatttagtag
<210> 442
<211> 362
<212> DNA
<213> Homo sapiens
<400> 442
ctaaggaatt agtagtgttc ccatcacttg tttggagtgt gctattctaa aagattttga 60
tttcctggaa tgacaattat attttaactt tggtggggga aagagttata ggaccacagt 120
cttcacttct gatacttgta aattaatctt ttattgcact tgttttgacc attaagctat 180
atgtttagaa atggtcattt tacggaaaaa ttagaaaaat tctgataata gtgcagaata 240
aatgaattaa tgttttactt aatttatatt gaactgtcaa tgacaaataa aaattctttt 300
tgattatttt ttgttttcat ttaccagaat aaaaactaag aattaaaagt ttgattacag 360
tc
                                                                   362
<210> 443
<211> 624
<212> DNA
<213> Homo sapiens
<220>
<221> misc_feature
<222> (1)...(624)
<223> n = A,T,C or G
<400> 443
tttttttttt gcaacacaat atacatcaca gtgaaatgtg taatccttgc aaattgcaag 60
ttgaaagaat taaattcaga ggaggggaga gaaagagtac tcagtaggga ctgagcacta 120
aatgettatt ttaaaagaaa tgtaaagage agaaageaat teaggetace etgeettttg 180
tgctggctag tactccggtc ggtgtcagca gcacgtggca ttgaacattg caatgtggag 240
```

```
cccaaaccac agaaaatggg gtgaaattgg ccaactttct attaacttgg cttcctgttt 300
 tataaaatat tgtgaataat atcacctact tcaaagggca gttatgaggc ttaaatgaac 360
 taacqcctac aaaacactta aacatagata acataggtgc aagtactatg tatctggtac 420
 atggtaaaca toottattat taaagtoaac gotaaaatga atgtgtgtgc atatgctaat 480
 agtacagaga gagggcactt aaaccaacta agggcctgga gggaaggttt cctggaaaga 540
ngatgettgt getgggteca aatettggte tactatgace ttggecaaat tatttaaact 600
 ttgtccctat ctgctaaaca gatc
<210> 444
 <211> 425
 <212> DNA ·
 <213> Homo sapiens
 <220>
 <221> misc_feature
 <222> (1)...(425)
<223> n = A,T,C or G
<400> 444
qcacatcatt nntcttgcat tctttgagaa taagaagatc agtaaatagt tcagaagtgg 60
quagetttgt ccaggeetgt gtgtgaacce aatgttttge ttagaaatag aacaagtaag 120
ttcattgcta tagcataaca caaaatttgc ataagtggtg gtcagcaaat ccttgaatgc 180
tgcttaatgt gagaggttgg taaaatcctt tgtgcaacac tctaactccc tgaatgtttt 240
gctgtgctgg gacctgtgca tgccagacaa ggccaagctg gctgaaagag caaccagcca 300
cctctgcaat ctgccacctc ctgctggcag gatttgtttt tgcatcctgt gaagagccaa 360
ggaggcacca gggcataagt gagtagactt atggtcgacg cggccgcgaa tttagtagta 420
gtaga
<210> 445"
 <211> 414
 <212> DNA
 <213> Homo sapiens
<220> ·
<221> misc_feature
 <222> (1)...(414)
 \langle 223 \rangle n = A,T,C or G
<400> 445
catgittatg nittiggatt actitigggca cotagigtti ctaaatcgic tatcaticti 60
ttctgttttt caaaagcaga gatggccaga gtctcaacaa actgtatctt caagtctttg 120
tgaaattctt tgcatgtggc agattattgg atgtagtttc ctttaactag catataaatc 180
tggtgtgttt cagataaatg aacagcaaaa tgtggtggaa ttaccatttg gaacattgtg 240
aatgaaaaat tgtgtctcta gattatgtaa caaataacta tttcctaacc attgatcttt 300
ggatttttat aatcctactc acaaatgact aggcttctcc tcttgtattt tgaagcagtg 360
tgggtgctgg attgataaaa aaaaaaaaag tcgacgcggc cgcgaattta gtag
                                                                    414
<210> 446
<211> 631
 <212> DNA
<213> Homo sapiens
 <220>
 <221> misc feature
<222> (1) ... (631)
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```
<223> n = A,T,C or G
 <400> 446
 acaaattaga anaaagtgcc agagaacacc acataccttg tccggaacat tacaatggct 60
 tctgcatgca tgggaagtgt gagcattcta tcaatatgca ggagccatct tgcaggtgtg 120
 atgctggtta tactggacaa cactgtgaaa aaaaggacta cagtgttcta tacgttgttc 180
 ccggtcctgt acgatttcag tatgtcttaa tcgcagctgt gattggaaca attcagattg 240
 ctgtcatctg tgtggtggtc ctctgcatca caagggccaa actttaggta atagcattgg 300
 actgagattt gtaaactttc caaccttcca ggaaatgccc cagaagcaac agaattcaca 360
 gacagaagca aaatacaggg cactacagtt cagacaatac aacaagagcg tccacgaggt 420
 taatctaaag ggagcatgtt tcacagtggc tggactaccg agagcttgga ctacacaata 480
 cagtattata gacaaaagaa taagacaaga gatctacaca tgttgccttg catttgtggt 540
 aatctacacc aatgaaaaca tgtactacag ctatatttga ttatgtatgg atatatttga 600
 aatagtatac attgtcttga tgttttttct g
 <210> 447
 <211> 585
 <212> DNA
<213> Homo sapiens
<220>
<221> misc_feature
<222> (1)...(585)
<223> n = A,T,C or G
<400> 447
ccttgggaaa antntcacaa tataaagggt cgtagacttt actccaaatt ccaaaaaggt 60
cctggccatg taatcctgaa agttttccca aggtagctat aaaatcctta taagggtgca 120.
gcctcttctg gaattcctct gatttcaaag tctcactctc aagttcttga aaacgagggc 180
agttcctgaa aggcaggtat agcaactgat cttcagaaag aggaactgtg tgcaccggga 240.
tgggctgcca gagtaggata ggattccaga tgctgacacc ttctggggga aacagggctg 300
ccaggtttgt catagcactc atcaaagtcc ggtcaacgtc tgtgcttcga atataaacct 360
gttcatgttt ataggactca ttcaagaatt ttctatatct ctttcttata tactctccaa 420
gttcataatg ctgctccatg cccagctggg tgagttggcc aaatccttgt ggccatgagg 480
atteetttat ggggteagtg ggaaaggtgt caatgggaet teggteteea tgeegaaaca 540
ccaaagtcac aaacttcaac teettggeta gtacaetteg gteta
<210> 448
<211> 93
<212> DNA
<213> Homo sapiens
<220>
<221> misc feature
<222> (1)...(93)
<223> n = A,T,C or G
<400> 448
tgctcgtggg tcattctgan nnccgaactg accntgccag ccctgccgan gggccnccat 60
ggctccctag tgccctggag agganggggc tag
                                                                  93
<210> 449
<211> 706
<212> DNA
<213> Homo sapiens
```

```
<220>
<221> misc_feature
<222> (1)...(706)
<223> n = A,T,C or G
<400> 449
ccaagttcat gctntgtgct ggacgctgga cagggggcaa aagcnnttgc tcgtgggtca 60
ttetgancae egaactgace atgecagece tgeegatggt cetecatgge teestagtge 120
cctggagagg aggtgtctag tcagagagta gtcctggaag gtggcctctg ngaggagcca 180
eggggacage atcetgeaga tggtegggeg egtoceatte gecatteagg etgegeaact 240
gttgggaagg gcgatcggtg cgggcctctt cgctattacg ccagctggcg aaagggggat 300
gtgctgcaag gcgattaagt tgggtaacgc cagggttttc ccagtcncga cgttgtaaaa 360
cgacggccag tgaattgaat ttaggtgacn ctatagaaga gctatgacgt cgcatgcacg 420
cgtacgtaag cttggatcct ctagagegge egectactae tactaaatte geggeegegt 480
cgacgtggga tccncactga gagagtggag agtgacatgt gctggacnct gtccatgaag 540
cactgagcag aagctggagg cacaacgene cagacactea cagetactea ggaggetgag 600
aacaggttga acctgggagg tggaggttgc aatgagctga gatcaggccn ctgcncccca 660
<210> 450
<211> 493
<212> DNA
<213> Homo sapiens
<400> 450
gagacggagt gtcactctgt tgcccaggct ggagtgcagc aagacactgt ctaagaaaaa 60
acagttttaa aaggtaaaac aacataaaaa gaaatateet atagtggaaa taagagagte 120
aaatgaggct gagaacttta caaagggatc ttacagacat gtcgccaata tcactgcatq 180
agcctaagta taagaacaac ctttggggag aaaccatcat ttgacagtga ggtacaattc 240
caagtcaggt agtgaaatgg gtggaattaa actcaaatta atcctgccag ctgaaacgca 300
agagacactg tcagagagtt aaaaagtgag ttctatccat gaggtgattc cacagtcttc 360
tcaagtcaac acatctgtga actcacagac caagttctta aaccactgtt caaactctgc 420
tacacatcag aatcacctgg agagetttac aaactcccat tgccgagggt cgacgcggcc 480
gcgaatttag tag
                                                                 493
<210> 451
<211> 501
<212> DNA
<213> Homo sapiens
<220>
<221> misc_feature
<222> (1) ... (501)
<223> n = A,T,C or G
<400> 451
gggegegtee cattegeeat teaggetgeg caactgttgg gaagggegat eggtgeggge 60
ctcttcgcta ttacgccagc tggcgaaagg gggatgtgct gcaaggcgat taagttgggt 120
aacgccaggg ttttcccagt cncgacgttg taaaacgacg gccagtgaat tgaatttagg 180
tgacnctata gaagagctat gacgtcgcat gcacgcgtac gtaagcttgg atcctctaga 240
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tggagagtga catgtgctgg acnctgtcca tgaagcactg agcagaagct ggaggcacaa 360
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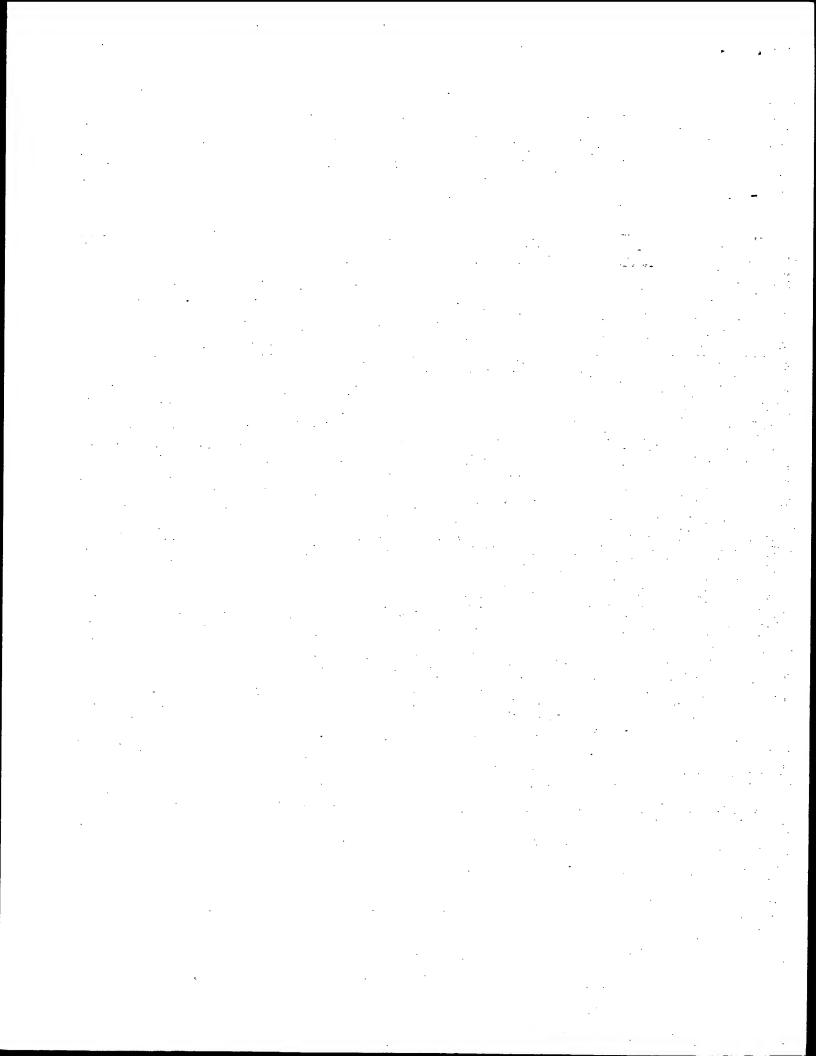
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agtagaaggt gattgccagg aaatggatct ggaaaagact cggagtgagc gtggagatgg 300
ctctgatgta aaagagaaga ctccacctaa tcctaagcat gctaagacta aagaagcagg 360
agatgggcag ccataagtta aaaagaagac aagctgaagc tacacacatg gctgatgtca 420
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cattgaaaat gtgactgaaa atttgaaaat tctctcaata aagtttgagt tttctctgaa 480 gaaaaaaaaa naaaaaaaa aaanaaaaan aaaaa 515



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(54) Title: COMPOSITIONS AND METHODS FOR THERAPY AND DIAGNOSIS OF PROSTATE CANCER

(57) Abstract

Compositions and methods for the therapy and diagnosis of cancer, such as prostate cancer, are disclosed. Compositions may comprise one or more prostate tumor proteins, immunogenic portions thereof, or polynucleotides that encode such portions. Alternatively, a therapeutic composition may comprise an antigen presenting cell that expresses a prostate tumor protein, or a T cell that is specific for cells expressing such a protein. Such compositions may be used, for example, for the prevention and treatment of diseases such as prostate cancer. Diagnostic methods based on detecting a prostate tumor protein, or mRNA encoding such a protein, in a sample are also provided.

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Internation No PCT/US 99/15838

CLASSIFICATION OF SUBJECT MATTER
C12N15/12 C07K14/47 A61K39/395 G01N33/68 C12Q1/68 IPC 7 C12N5/02 C12N15/62 G01N33/574 C07K16/30 //A61P35/00 According to International Patent Classification (IPC) or to both national classification and IPC Minimum documentation searched (classification system followed by classification symbols) C12N C07K IPC 7 Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched Electronic data base consulted during the international search (name of data base and, where practical, search terms used) C. DOCUMENTS CONSIDERED TO BE RELEVANT Citation of document, with indication, where appropriate, of the relevant passages Relevant to claim No. Category 1-22, WO 97 33909 A (CORIXA CORP) 18 September 1997 (1997-09-18) 29-31, 35-49, 53-79 the whole document 23-28, SJOGREN H 0: "Therapeutic immunization A 32-34, against cancer antigens using genetically 53-57 engineered cells" IMMUNOTECHNOLOGY, vol. 3, no. 3, 1 October 1997 (1997-10-01), pages 161-172, XP004097000 ISSN: 1380-2933 the whole document Further documents are listed in the continuation of box C. Patent family members are listed in annex. X Special categories of cited documents: "T" later document published after the international filing date or priority date and not in conflict with the application but "A" document defining the general state of the art which is not cited to understand the principle or theory underlying the considered to be of particular relevance invention earlier document but published on or after the international "X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to filing date involve an inventive step when the document is taken alone "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another "Y" document of particular relevance; the claimed invention citation or other special reason (as specified) cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled "O" document referring to an oral disclosure, use, exhibition or in the art. document published prior to the international filing date but \*&" document member of the same patent family later than the priority date claimed Date of mailing of the international search report Date of the actual completion of the international search 0 4. 05. 00 31 January 2000 Authorized officer Name and mailing address of the ISA European Petent Office, P.B. 5818 Patentiaan 2 NL - 2280 HV Riswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl. ANDRES S.M. Fax: (+31-70) 340-3016

International Application No PC1, JS 99/15838

1		PC1/03 39/13030
C.(Continua	tion) DOCUMENTS CONSIDERED TO BE RELEVANT	
Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
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A	EP 0 317 141 A (BECTON DICKINSON CO) 24 May 1989 (1989-05-24) the whole document	50-52
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P,X	WO 98 37093 A (CORIXA CORP) 27 August 1998 (1998-08-27)  page 3, line 20 -page 22, line 2 page 35, line 9 - last line page 76, line 34 -page 78, line 22 claims	1-15, 17-19, 21,22, 29-31, 34,35, 39-42, 44-46, 48,49, 58-79
P,X	Page 2 -page 24 example 2 page 35, line 15 -page 36, line 11 page 81, line 14 -page 83, line 11 claims	1-15, 17-19, 21,22, 29-31, 34,35, 39-42, 44-46, 48,49, 58-79

ational application No.

PCT/US 99/15838

Box	Observations where certain claims were found unsearchable (Continuation of Item 1 of first sheet)
This Inte	emational Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:
<u> </u>	
1. [X]	Claims Nos.: because they relate to subject matter not required to be searched by this Authority, namely:
	Remark: Although claims 29-34, 48-49, 52, 55-57
•	are directed to a method of treatment of the human/animal
	body, the search has been carried out and based on the alleged effects of the compound/composition.
. (—	
2 📋	Claims Nos.: because they relate to parts of the International Application that do not comply with the prescribed requirements to such
	an extent that no meaningful International Search can be carried out, specifically:
3	Claims Nos :
• —	because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).
Box II	Observations where unity of invention is lacking (Continuation of item 2 of first sheet)
	mational Searching Authority found multiple inventions in this international application, as follows:
see	e additional sheet
•	
) .	
1.	As all required additional search fees were timely paid by the applicant, this International Search Report covers all
· . •	searchable claims.
2	As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
	any unamontal ros.
3 [	As only some of the required additional search fees were timely paid by the applicant, this International Search Report
ا ا	covers only those claims for which fees were paid, specifically claims Nos.:
•	
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4. X	to required additional search fees were timely paid by the applicant. Consequently, this International Search Report is estricted to the invention first mentioned in the claims; it is covered by claims Nos.:
1	1-79 all partially
Remark o	n Protest The additional search fees were accompanied by the applicant's protest.
	No protest accompanied the payment of additional search fees.

#### FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Invention 1. Claims: 1-79 (all partially)

A polypeptide comprising at least an immunogenic portion of a prostate tumor protein defined as SEQ ID 108 and which is encoded by the related SEQ IDs 2,3,107 (according to the Description of the Sequence Identifiers), fragments and variants thereof, fusion proteins comprising it, polynucleotides or oligonucleotides derived therefrom, antibodies or fragments thereof binding to the polypeptide, pharmaceutical compositions or vaccines comprising these products and their use in methods for inhibiting, monitoring or diagnosing the development of a prostate cancer, for removing tumor cells from a sample or for expanding and/or stimulating T-cells.

Inventions 2. to 439. Claims: 1-79 (all partially and as far as applicable)

As for subject 1. but concerning respectively SEQ IDs 1,4-106,109-111,115-171,173-175,177,179-305,307-315,326,328,330,332-335,340-375,381,382 and 384-472.

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